CORRELATION OF BUN/CREATININE RATIO WITH OUTCOME IN ACUTE STROKE

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Submitted By

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I hereby declare that the thesis entitled **"CORRELATION OF BUN/CREATININE RATIO WITH OUTCOME IN ACUTE STROKE''** submitted towards partial fulfillment of the requirements for the award of **MD in Medicine** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Dinesh Jain**, Professor, Department of Medicine, **Dr. Birinder Singh Paul**, Professor, Department of Neurology and **Dr. Amit Bery**, Associate Professor, Department of Medicine. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

my Family

&

Teachers

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Dr. Amandeep Kaur

LIST OF ABBREVIATIONS

AIS	Acute Ischemic Stroke
BI	Barthel Index
BUN	Blood Urea Nitrogen
CT	Computed Tomography
CKD	Chronic Kidney disease
DALY	Disability-Adjusted Life-Years
eGFR	Estimated Glomerular Filtration Rate
END	Early Neurological Deterioration
FLAIR	Fluid-Attenuated Inversion Recovery
FOIS	Functional Oral Intake Scale
GBD	Global Burden of Disease
GCS	Glasgow Coma Scale
HVs	Hyperintense Vessels
MCA	Middle Cerebral Artery
MRA	Magnetic Resonance Angiography
MRI	Magnetic Resonance Imaging
mRS	Modified Rankin Scale
NIHSS	National Institute of Health Stroke Scale
OR	Odds Ratio
PCA	Posterior Cerebral Artery
SDI	Socio-Demographic Index
SIE	Stroke-in-Evolution
USG	Urine Specific Gravity
VCS	Volume Contracted State
WHO	World Health Organisation

ABSTRACT

Introduction: Stroke is becoming an important cause of premature death and disability in low-income and middle-income countries like India. Hydration status at the time of stroke has been acknowledged as an important determinant in early stroke recovery and outcome factor.

Aim: The present study was designed to determine the association between BUN/Creatinine ratio, a marker of relative dehydration and the outcome in acute stroke.

Materials and Methods: A total of 116 patients admitted in DMC&H with the diagnosis of stroke during the period from January 2020 to December 2020, were included in the study. Demographic characteristics, stroke type, baseline GCS (12 or ≤12) and NIHSS score (≥12 or 12), BUN/Cr ratio (>15 or ≤15) and other laboratory variables were studied as predictors of outcome in acute stroke. Outcome was assessed by mRS score at day 30. Good outcome was defined by patients having mRS score ≤ 2 and poor outcome when the mRS score was >2 at day 30 (death/dependency).

Results: Of the 116 patients enrolled in the study, 88.7% had ischaemic stroke while 11.2% had haemorrhagic stroke. The mean age (±SD) was 61.35 (±11.14) years. In the present study, males (54.3%) were more as compared to females (45.7%). The variables associated with poor outcome were: age > 60 years, baseline GCS ≤12, NIHSS ≥12 at admission, haemorrhagic stroke, BUN/creatinine >15, USG >1.010 and prolonged hospital stay (>10 days). On multivariate analysis, BUN/creatinine >15 and prolonged hospital stay (>10 days) were found to be independent predictor of poor outcome. Acute ischaemic stroke with admission dehydration, defined by BUN/creatinine >15 showed worse outcome mRS score at 30 days while no such association was seen in acute haemorrhagic stroke($p<0.001$).

Conclusion: In our study, BUN/Creatinine >15 was found as an independent predictor of poor outcome. Hence, monitoring of the hydration status needs to be emphasized in the management of acute stroke patients.

Keywords: Blood urea nitrogen/Creatinine ratio, acute stroke, mRS, outcome.

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INTRODUCTION

The current World Health Organization definition of stroke is “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.” Ischaemic strokes are defined as all atherosclerotic and thromboembolic events that resulted in compromised blood flow to brain tissue and subsequent infarction. Haemorrhagic strokes are defined as all non-traumatic events due to subarachnoid or intracerebral haemorrhage identified by neuroimaging.[1]

Approximately 56 million deaths occur annually worldwide, with approximately one-quarter of these deaths attributable to vascular disease. Ischemic heart disease (7.2 million deaths annually) and stroke (5.5 million deaths annually) represent the top two causes of mortality globally. Stroke in particular accounts for approximately 9.7% of all deaths worldwide and it remains one of the most devastating of all neurological conditions. Worldwide it accounts for approximately 5.5 million deaths annually, with 44 million disability-adjusted life-years lost. Globally, an estimated 16 million people suffered from a first-ever stroke in the year 2005, with an estimated prevalence of 62 million stroke survivors. In the absence of any meaningful clinical or public health interventions, it is expected that this number will increase to an estimated 23 million first-ever strokes, with an associated 7.8 million deaths, by 2030.[2,3]

Stroke, a highly prevalent condition, exacts a substantial societal toll in the form of the “Dreaded-D’s,” which are the leading cause of chronic disability, the second leading cause of dementia, and the fourth leading cause of death in the United States (U.S.). The worldwide impact of stroke seems to be even more pronounced than it is in the U.S. In the U.S., the prevalence of stroke is roughly 3% of the adult population, which translates to approximately 7 million individuals. Of these strokes, approximately 87% are ischemic infarctions, 10% are primary

hemorrhages, and 3% are subarachnoid hemorrhage. Worldwide estimates indicate that primary hemorrhages constitute a higher percentage of all strokes, ranging from 10% to 25%. Individuals of Asian, African, and Latin American origin tend to have a higher frequency of primary hemorrhage than persons of European origin.[4]

Pandian et al studied the burden of stroke and the availability of health Services in India. The estimated adjusted prevalence rate of stroke ranges 84-262/100,000 in rural and 334-424/ 100,000 in urban areas. The incidence rate is 119-145/100,000 based on the recent population-based studies. There was a wide variation in case fatality rates with the highest being 42% in Kolkata.[5]

Longitudinal studies have identified several characteristics/conditions that boost a person's risk for primary or recurrent stroke. An international case-control study (i.e., the INTERSTROKE study) of 3000 stroke cases, and corresponding number of controls, showed that roughly 90% of strokes could be explained by 10 risk factors: 1) hypertension, 2) diabetes, 3) cardiac causes, 4) current smoking, 5) abdominal obesity, 6) hyperlipidemia, 7) physical inactivity, 8) alcohol consumption, 9) diet, and 10) psychosocial stress and depression.[6]

In acute stroke, the fate of the ischaemic penumbra directly depends on the severity and duration of ischaemia. During this potentially unstable period, physiological factors such as homeostatic disturbances and haemostatic activation (e.g., excessive thrombin generation, fibrin turnover) can exacerbate neuronal death. Early neurological deterioration is a frequent and important complication in acute stroke, occurring in 26–43% of patients, and about half of all cases occur within 24 h of admission. END is more likely to be associated with hemodynamic and metabolic causes, whereas late deterioration is most often due to systemic complications such as infection and aspiration or to stroke recurrence.[7]

A large percentage of stroke patients are dehydrated at the time of stroke and appear to have worsened functional outcomes. Dehydration

might adversely affect the acute stroke patient in several ways: (1) reduced brain perfusion (2) increased fatigue (3) impaired neuroplasticity. During the early stroke recovery period, autoregulatory systems are impaired, leaving the brain vulnerable to blood viscosity and pressure changes that could further injure the area already compromised by decreased oxygen and nutrients.[8] Dehydration increases blood viscosity and is felt to diminish cerebral blood flow due to lower intravascular volume. Elevated hematocrit has been shown to be associated with a larger infarct volume in patients with cerebral infarction.[9]

Dehydration is not an uncommon finding of patients presenting to an emergency department with an overall prevalence of 7%. It is more common in elderly patients with one estimate suggesting that 1.5% of independent elderly patients will be admitted for dehydration annually and evidence of chronic dehydration can be seen in almost half of geriatric patients presenting to emergency departments for care.[10,11] Elderly patients are more susceptible to dehydration as they are more likely to have physical barriers to self-hydration, are more likely to be on medications that promote dehydration such as diuretics, have diseases that increase water loss such as diabetes and show decrease thirst sensation. Thirst drive decreases with age, leaving the older population vulnerable to high rates of dehydration.[12]

Rodriguez et al[13] have observed that the elderly patients presenting with transient ischaemic attack or acute ischaemic stroke often demonstrate increased plasma osmolality, likely representing a volume depleted state, and possibly contributes to cerebral ischaemia and poor neurological outcome. The role of volume depletion or dehydration as a risk factor contributing to Early neurological deterioration was further studied by Lin et al[14] who demonstrated that blood urea nitrogen/ creatinine (BUN/Cr) ratio higher than 15 was more frequently seen in SIE (Stroke in Evolution) patients.

Hydration status at the time of stroke has been acknowledged as an important determinant in early stroke recovery. Biochemical parameters like plasma osmolality, BUN/creatinine ratio and urine specific gravity have been used by various investigators for assessment of hydration status. Amongst these, the blood urea nitrogen (BUN) to creatinine (Cr) ratio (BUN/Cr) is a commonly used parameter to assess dehydration status, especially in patients with normal renal function.[8,15] The present study was designed to determine the association between admission dehydration status, defined by BUN/Creatinine ratio >15 and the outcome in patients with acute stroke.

AIMS AND OBJECTIVES

- To correlate BUN/Creatinine ratio, a marker of relative dehydration with the outcome in acute stroke.

REVIEW OF LITERATURE

Stroke is becoming an important cause of premature death and disability in low - income and middle-income countries like India, largely driven by demographic changes and enhanced by the increasing prevalence of the key modifiable risk factors. As the epidemiological transition of diseases extends through developing countries around the world, the gross number of global deaths attributable to stroke is expected to increase exponentially.[2]

Global Burden of Disease (GBD) 2016 study estimates to provide global, regional, and country-specific lifetime risk of stroke in 1990 and 2016 by pathological subtype, age, sex and Socio-Demographic Index (SDI), accounting for competing risk of mortality due to all other non-stroke causes of death. The global estimated lifetime risk of stroke from age 25 onward was 24.9%: 24.7% in men and 25.1% in women. Globally from 1990 to 2016, there was a significant increase in the average lifetime risk of stroke from 22% to 24%, a relative increase of 9% with the change in the risk of ischemic stroke exceeding that of haemorrhagic stroke. Stroke accounts for almost 5% of all disability-adjusted life-years and 10% of all deaths worldwide, with the bulk of this burden (>75% of deaths from stroke and >80% of disability-adjusted life-years) occurring in low-income and middle-income countries.[3]

As a disease of aging, the prevalence of stroke is expected to increase significantly in the years ahead as the global population older than 65 years of age continues to increase by approximately 9 million people per year. By 2025, the global population of people older than the age of 65 years is estimated to be approximately 800 million people and two-third of them are expected to live in still-developing countries, particularly in Latin America and Asia.[2] The incidence of stroke rapidly increases with age, doubling for each decade after the age of 55 years. Among adults ages 35 to 44, the incidence of stroke is 30 to 120 of

100,000 per year, and for those ages 65 to 74, the incidence is 670 to 970 of 100,000 per year.[4]

Kwan J et al study observed that patients with early neurological deterioration were significantly more likely to: (i) arrive at the hospital earlier (ii) have a history of atrial fibrillation (iii) be current non-smokers (iv) have a severe stroke-more total anterior circulation strokes and worse NIHSS and GCS scores; (v) have intracerebral haemorrhage (vi) have higher serum urea and leukocyte count and (vi) die in hospital .Serum urea level and leukocyte count were higher amongst patients with early neurological deterioration, which suggests that it might induce a greater level of systemic inflammatory response, or lead to physiological sequelae including dehydration (e.g. reduced oral intake secondary to dysphagia and reduced consciousness).[7]

Mona N. Bahouthet al conducted Twenty-five studies of 8699 acute stroke patients. Nineteen studies reported on the diagnostic approach to dehydration. Overall, rates of dehydration in the acute stroke ranged from 29 to 70% using a variety of measurement techniques. The most common laboratory marker used in these studies was blood urea nitrogen to creatinine ratio (BUN/Cr) which was used in 12 studies. Of the 12 studies reporting patient outcomes, 10 (83%) reported poor clinical outcomes in dehydrated stroke patients.[8]

The functional consequences of dehydration during the early stroke recovery period could include: increased rates of delirium, poor concentration, increased fatigue, or positional hypotension. These early functional consequences may be crucial since neuroplasticity is thought to peak in the first several weeks after stroke, so engagement in physical therapy during this limited period is critical. Hence, Hydration status at the time of stroke has been acknowledged as an important determinant in early stroke recovery.[8]

Schrock JW et al studied association of elevated BUN/Creatinine with outcome in AIS. The variables associated with a poor neurological outcome were: high NIHSS OR 6.5 (3.6-11.8), age >64 years OR 2.7

(1.5-5.0), and BUN/Cr ratio of ≥15 OR 2.2 (1.2-4.0). Adequate hydration status is important to maintain physiological homeostasis in humans. The brain is able to control cerebral blood flow through autoregulation allowing constant cerebral perfusion pressure despite moderate variations of blood pressure. Dehydration has been shown to blunt cerebral autoregulatory response to orthostatic positioning but did not lower cerebral perfusion overall.[9]

Many factors are known to influence the hydration status; e.g., advanced age with decreased thirst sensation or diabetes mellitus with increased diuresis. Although in conscious individuals without physical limitations thirst sensation ultimately leads to volume replacement when fluid is available. The elderly, the fastest growing population, despite adequate fluid consumption, demonstrate decreased thirst sensation and delayed fluid restoration. With increasing age, especially above 65 years, there is decreased THIRST sensation and decreased glomerular filtration rate with altered ability to concentrate urine. Reduced fluid intake and delayed restoration is commonly seen in elderly persons after exercise, with fluid restrictions, or in warm environments. Dehydration regardless of its cause may precipitate cerebral ischemic events in susceptible elderly individuals. Dehydration also has been linked to higher risk of recurrent embolization in patients with atrial fibrillation.[12,13]

Rodriguez GJ et at study observed a higher plasma osmolality among elderly patients with cerebral ischaemic events who present within 24 hours of symptom onset compared with controls from the general population. Patients taking diuretics had higher plasma osmolality than patients not taking diuretics (296.0 ± 8.0 vs. 292.4 ± 8.0 mOsm/ kg, P = 0.0026). Among patients, there was no difference between subgroups defined by stroke subtypes or time from symptom onset. This supports the proposition that high plasma tonicity, a marker of dehydration, is a potential contributing factor to cerebral ischemia.[13]

Three possible mechanisms may explain the relationship between high plasma osmolality and cerebral ischemic events. First, high osmolality representing a dehydration state, may manifest as orthostatic intolerance and decreased cerebral blood flow with orthostatic changes. In the case of underlying vascular pathology such as intracranial or cervical arterial narrowing, hypovolemia could lead to ischemia or infarction.[13]

Second, high osmolality representing a dehydration state leads to an increase in blood viscosity. Hematocrit is the major determinant of blood viscosity and increases when intravascular volume decreases. The Hagen-Poiseuille equation states that high viscosity translates into an impaired cerebral blood flow. An elevated hematocrit has been associated with an increased risk for ischemic stroke related to cardioembolism, and large and small-vessel disease.[13,16,17]

Third, it has been hypothesized that dehydration could trigger the coagulation cascade by activating the sympathetic autonomic system. Dehydration has been shown to be associated with recurrent embolic stroke and thrombotic events including venous thromboembolism after an acute stroke[18] and it was also found to be associated with intra-cardiac clot progression in patients with a history of cardioembolic stroke.[19]

Lin LC et al study observed that an initial National Institutes of Health Stroke Scale score of 12 or higher, a Glasgow Coma Scale score of 12 or lower, d-dimers more than 1000, or blood urea nitrogen/creatinine (BUN/Cr) ratio higher than 15 were more frequent in SIE (stroke in evolution) patients. After multivariate analysis, only a BUN/Cr higher than 15 was independent predictor of SIE. These findings suggest that BUN/Cr may be a novel predictor of SIE, potentially useful in emergency departments.[14]

Bhatia K et al study observed that National Institutes Health Stroke Scale score (NIHSS) ≥ 12 at admission is an independent risk factor for END (Early neurological deterioration). Amongst markers of relative

dehydration, BUN/creatinine >15 at admission was found to be an independent risk factor for END, as also USG >1.010. Patients with stroke are often at increased risk of dehydration as they have a reduced level of consciousness, are physically dependent, unable to communicate, have difficulties in swallowing and decreased oral intake.[15]

Chang SW et al studied the association of development of leptomeningeal collaterals after acute MCA occlusion with the patient's hydration status. Eighty-seven patients with acute infarction due to occlusion of the MCA were enrolled. Amongst them, 61 (70.1%) were dehydrated with BUN/Cr ratio ≥15. Two imaging markers, prominent laterality of PCA on magnetic resonance angiography (MRA) and hyperintense vessels (HVs) on fluid-attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI), were used to assess the collateral circulation after acute MCA occlusion. The development of PCA laterality and HVs shows a significant difference between dehydrated and euhydrated patients. Dehydration remained an independent negative predictor for the development of PCA laterality and HVs in the multivariate analysis.[20]

Dehydration would lower the overall and cerebral blood volume, the blood velocity as well as the intravascular pressure that results in a lower pressure gradient and the ability to stimulate collateral recruitment. The development of collateral flow after occlusion of major arteries can sustain brain tissue for hours and may play a role in maintaining perfusion in the penumbral region.[20,21]

Neuronal damage is not uniform when a cerebral artery is occluded, especially in the first few hours after the insult. This duration depends on the development and extension of collateral perfusion and may not be complete for hours or even days. Dehydration has been proposed to be one of the conditions that might adversely affect collateral circulation.[22] Early hydration therapy is necessary for the development and maintenance of collaterals in dehydrated patients, thus maintaining

the penumbra by promoting collaterals, and enhance the effect of reperfusion therapy. For patients with poor collaterals, the time window for reperfusion therapy may be shorter, and for this reason a more immediate and intensive reperfusion treatment is necessary.[23]

Bahouth, Mona N et al studied the relationship between a volume contracted state (VCS) at the time of ischemic stroke and hospital outcomes as compared with euvolemic patients. Acute stroke patients in a VCS demonstrate worse short-term outcomes compared to euvolemic patients, independent of infarct size. VCS was defined via surrogate markers (blood urea nitrogen/creatinine ratio >15 and urine specific gravity >1.010). 42% of patients in a VCS demonstrated early clinical worsening, compared with 17% of the euvolemic group ($p = 0.02$).[24]

Though yet unproven, there are several biological theories about why a Volume contracted state (VCS) at the time of stroke could influence functional outcome. These include reduction of cerebral perfusion during critical periods of failing autoregulation, increased overall viscosity disrupting microcirculatory pathways, and the dilution and circulation of inflammatory cells that may accelerate cerebral edema in the region of infarction. A growing body of evidence suggests a relationship between dehydration and poor outcome measured by risk for neurologic fluctuation, worsened hemispatial neglect, increased hospital complications, and hospital disposition after stroke.[9,14]

Mohammad Dehghani - Firoozabadi et al conducted a prospective study across a 30-month period commencing on 23rd September 2009 to evaluate the relationship between Blood BUN, creatinine (Cr), BUN/Cr ratio and mortality in patients with stroke. Patient-specific demographic information, serum BUN, Cr, BUN/Cr ratio and outcome data related to each presentation was recorded. Patients who succumbed to Stroke (early death or late death) had significantly higher mean BUN, BUN/Cr levels than those who survived. This correlation of

hyperuremia and mortality suggests that it may be useful in guiding risk assessment and treatment of stroke.[25]

Zheng D et al compared the prognostic significance of BUN and other CKD biomarkers (eGFR, Cr and BUN/Cr) in in-hospital mortality and poor discharge outcomes after AIS. A total of 3,355 AIS patients were enrolled from December 2013 to May 2014, across 22 hospitals. There were 1,287 patients with poor outcome (mRS score ≥3) at hospital discharge. Patients with higher BUN (≥6.70mmol/l) appeared to have a 3.75-fold increase in the risk of in-hospital mortality after adjustment for potential confounders, including eGFR.[26]

Liu CH et al studied the influence of admission dehydration on the discharge outcome in acute ischaemic and hemorrhagic stroke. In total, 2570 acute ischaemic and 573 acute hemorrhagic stroke patients were recruited. Acute ischaemic stroke with admission dehydration had higher infection rates, worse discharge Barthel index (BI), worse mRS and higher admission costs than those without dehydration. Blood urea nitrogen (BUN) to creatinine (Cr) ratio (BUN/Cr) was commonly used parameter to assess dehydration status.[27]

Bahouth MN et al study observed that patients who are in a volume contracted state at the time of presentation with stroke have more severe hemispatial neglect. The primary definition of a VCS was a BUN/creatinine ratio >15, with secondary definition including urine specific gravity >1.010. Of 201 patients meeting inclusion criteria, 131/201 (65%) had elevated BUN/creatinine ratios at admission. Approximately 61% (122/201) had some degree of neglect. Elevated BUN/Creatinine ratio was associated with an increased odds of severe neglect in unadjusted models, with loss of significance in adjusted models (OR 4.43, (95% CI 0.99, 19.8) after adjustment for age, infarct volume, sex, and NIHSS score.[28]

Rowat A et al study observed that patients with dehydration within 1 day of admission and those with dehydration at any stage of their admission were both significantly more likely to be older, to be female,

to have a total anterior circulation syndrome, to be prescribed diuretics, to require parenteral fluids and/or enteral tube feeding, and were predicted to be less likely to be alive/independent in daily activities at 6 months (based on their baseline features) than those who were not dehydrated.(16) Of the 2591 patients, 927 (36%) were dehydrated during their first blood test performed on the day of admission or the day after, another 679 (26%) were not dehydrated on admission but had at least 1 blood test indicating dehydration at some point during their admission, and 985 (38%) had normal hydration during their whole admission.[29]

Bhalla A et al studied the association of raised plasma osmolality on stroke outcome at 3 months and the change of plasma osmolality with hydration during the first week after stroke. Mean admission (300 mOsm/kg, SD 11.4), maximum (308.1 mOsm/kg, SD 17.1), and Area under curve (298.3 mOsm/kg, SD 11.7) plasma osmolality were significantly higher in those who died compared with survivors. After adjustment for age, sex, subtype, and stroke severity, study demonstrated that raised plasma osmolality, defined as >296 mOsm/kg on admission, was independently related to mortality.[30]

Churchill et al observed that stroke patients with stable renal function and high BUN levels were often medicated with diuretics, whereas Kelly et al reported that dehydration in the days immediately after acute ischemic stroke was associated with an increased BUN/Cr ratio and a predisposition for venous thromboembolism. This indicates that stroke patients with a higher BUN/Cr ratio may be at risk of early deterioration specifically due to an increased risk of venous thromboembolism. Hence, an immediate intervention for such patients should be the maintenance of proper hydration.[18,31]

Bhatia R S et al studied the prognostic value of various clinical, hematological and biochemical parameters in patients of acute stroke, on fatality occurring during the first 30 days. A total of 116 consecutive patients (77 males and 39 females) of stroke (within 72 hours of onset)

were included. The patients were followed up for a maximum period of 30 days from the onset of stroke. Among hematological parameters, high total leukocyte count and ESR, at admission, correlated significantly with an undesirable outcome during the initial 30 days. Among biochemical parameters, elevated urea, creatinine, serum transaminases (SGOT and SGPT) and globulin levels correlated significantly with death.[32]

Alawneh JA et al studied Hemodynamic factors and perfusion abnormalities in anterior circulation ischemic stroke. Infarction of the oligemic tissue surrounding the penumbra could be the putative culprit leading to END as a result of perfusion, but also physiological and biochemical abnormalities.[33]

Crary MA et al studied nutrition and hydration status in ischemic stroke patients with versus without clinically significant dysphagia at admission and at discharge from acute care. At admission 32 % of patients demonstrated malnutrition based on prealbumin levels and 53 % demonstrated evidence of dehydration based on BUN/Cr levels. Patients with dysphagia demonstrated significantly higher BUN/Cr levels (greater dehydration) than patients without dysphagia at admission and at discharge. Bun/Cr levels at baseline demonstrated a significant inverse correlation with stroke impairment (BI). At discharge, Bun/Cr values were significantly inversely correlated with FOIS and stroke impairment (BI), and significantly positively correlated with stroke severity as measured by the NIHSS. Dehydration has been associated with poststroke complications and 3month mortality following stroke.[34]

The process of secondary neuronal damage can occur very quickly after the initial stroke, and any attempts to halt the process should be made aggressively and urgently. Dehydration after stroke is associated with increased BUN/creatinine ratio, decreased blood pressure, increase in blood viscosity, reduced circulation in collaterals and predisposition for venous thromboembolism; the factors that may

worsens the ischaemic process. Acute stroke unit care should be characterized by intensive physiological monitoring and correction of abnormal parameters such as fever, hyperglycaemia, hypoxia, and dehydration. Studies suggest that this ‘intensive’ style of stroke unit care could almost half the number of deaths within the first 3 weeks (from 14% to 8%), and it has been suggested that this could be a result of preventing early neurological deterioration.[15,18,20,35]

MATERIAL AND METHODS

The study was conducted in the Department of Medicine at Dayanand Medical College and Hospital, Punjab, India from January 2020 to December 2020. It was an observational prospective study in which 116 consecutive patients presenting to the Emergency department with the diagnosis of stroke and after fulfilling the inclusion and exclusion criteria were included in the study.

INCLUSION CRITERIA

- Age > 18 years
- Acute stroke (ischaemic / hemorrhagic) < 24 hours duration
- Patient/attendant willing to give informed written consent

EXCLUSION CRITERIA

- Stroke > 24 hours duration
- Transient ischaemic attack
- Stroke mimics
- Congestive cardiac failure
- Chronic kidney disease
- Decompensated cirrhosis of liver

METHOD OF COLLECTION OF DATA

A detailed history was taken and a thorough general physical and systemic examination was performed. The following details were collected: age; sex; signs and symptoms; baseline GCS and NIHSS score, history of diabetes, hypertension, coronary artery disease, dyslipidemia, pre-existing diuretic use and any addiction. Laboratory investigations comprising complete blood count, blood urea, serum creatinine, BUN/creatinine ratio, serum electrolytes, blood glucose at admission, lipid profile, urine specific gravity, brain imaging and electrocardiogram were performed within 24hour of admission in all the patients. Since BUN reflects only the nitrogen content of urea (MW 28) and urea measurement reflects the whole of the molecule (MW 60), urea is approximately twice (60/28 = 2.14) that of BUN. Following

formula was used, Urea [mg/dL] = BUN [mg/dL] * 2.14. Factor = 1 for conversions in mmol (1 mole N_2 = 2 moles N per mole of urea). Serum creatinine was determined using the Autopak® reagent kit which utilizes the alkaline picrate Jaffe's reaction method. The analytical CV for measuring creatinine was 21.1 per cent. According to the BUN/Cr ratio, patients were divided into dehydrated (BUN/ Cr ≥ 15) and non-dehydrated (BUN/Cr < 15) subgroups.

The neurological status of the patient and the severity of stroke were assessed by using the GCS and NIHSS scoring system. All patients underwent a neuroimaging (NCCT/MRI brain) on admission and the findings were interpreted by a radiologist. The hospital course of all the admitted patients were analysed with respect to the need for ICU care (the ICU admission were done as per the hospital protocol) and duration of hospital stay.

TABLE 1: Neurological disability assessed by using modified ranking scale (mRS)

mRS SCORE	Clinical description
0	No symptom
1	No significant disability
2	Slight disability
3	Moderate disability; requires some help
4	Moderately severe disability
5	Severe disability
6	dead

Outcome was assessed by mRS score at the time of discharge or day 7 and on day 30. The mRS score on day 30 was confirmed by telephonic conversation with the patient/ relative of the patients. The patients were divided into two groups based on mRS score on day 30. Patients with mRS score ≤ 2 means though they had some disability but were still independent in their activities and mRS score > 2 suggests dependency/ death. Good outcome was defined by patients having mRS score ≤ 2 and poor outcome when the mRS score at day

30 was >2. Demographic characteristics, clinical characteristics, baseline GCS (12 or ≤ 12) and NIHSS score (≥12 or 12), stroke type, BUN/Cr ratio (>15 or ≤ 15), duration of hospital stay and other variables were compared.

STATISTICAL ANALYSIS

The data were compiled and analysed using standard statistical methods and relevant conclusions were drawn using a computer-based software SPSS version 16.0. Continuous data were expressed as mean ± standard deviation (SD) and were compared using Student t test for normally distributed variables and Mann Whitney U test for non-parametric data. Categorical data were expressed as frequencies and percentages, and were compared using chi-square test and Fisher's Exact test, wherever applicable. The data were analysed by univariate and multivariate analysis. The correlation between variables was ascertained using Pearson's correlation coefficient for normally distributed data and Spearman's coefficient for non-parametric data. A probability value (p value) less than 0.05 was considered statistically significant.

OBSERVATION AND RESULTS

A total number of 116 patients were included in the study. We analyzed demographical, various clinical and biochemical parameters along with stroke severity in patients with acute stroke presenting to the Emergency department during 2020. Their final outcome was assessed by mRS score at day 30.

TABLE 2: DISTRIBUTION OF PATIENTS ACCORDING TO AGE

Age group (years)	No. of cases (n=116)	Percentage
< 40	4	3.4%
41-50	16	13.8%
51-60	41	35.3%
> 60	55	47.4%
Total	116	100.0%

In our study, 47.4% (55 patients) were more than 60 years of age, 35.3% (41 patients) belonged to the age group between 51 to 60 years and 13.8% (16 patients) belonged to age group between 41 to 50 years. There were 3.4% (4 patients) below the age of 40 years. The mean age of presentation was 61.35 (+/- 11.14) years.

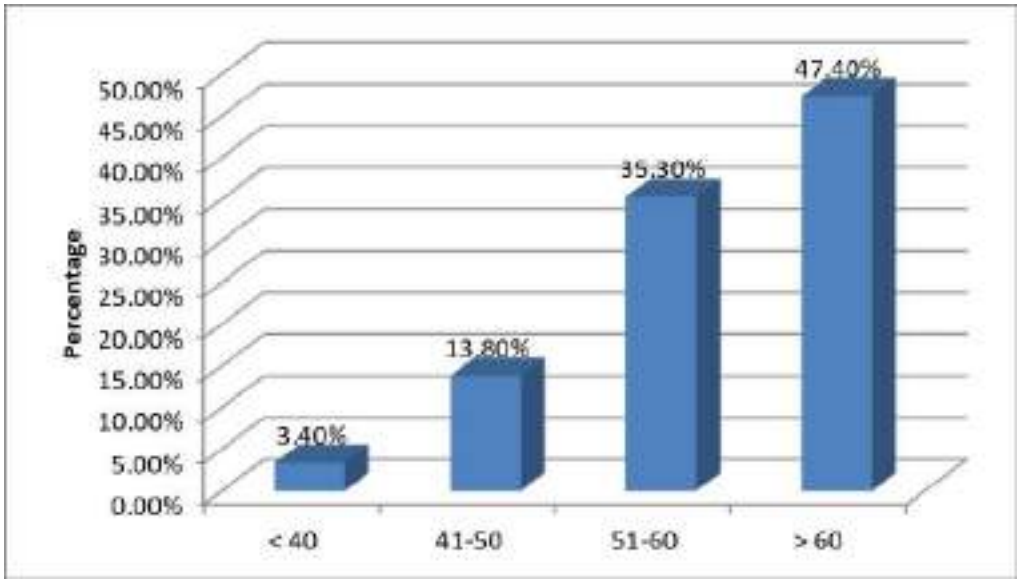

FIGURE 1: DISTRIBUTION OF PATIENTS ACCORDING TO AGE

TABLE 3: DISTRIBUTION OF PATIENTS ACCORDING TO GENDER

GENDER	No. of cases (n=116)	Percentage
Female	53	45.7%
Male	63	54.3%
Total	116	100.0%

In our study of 116 patients, 63 (54.3%) patients were males and 53 (45.7%) were females. In our study, males were more as compared to females with the diagnosis of stroke.

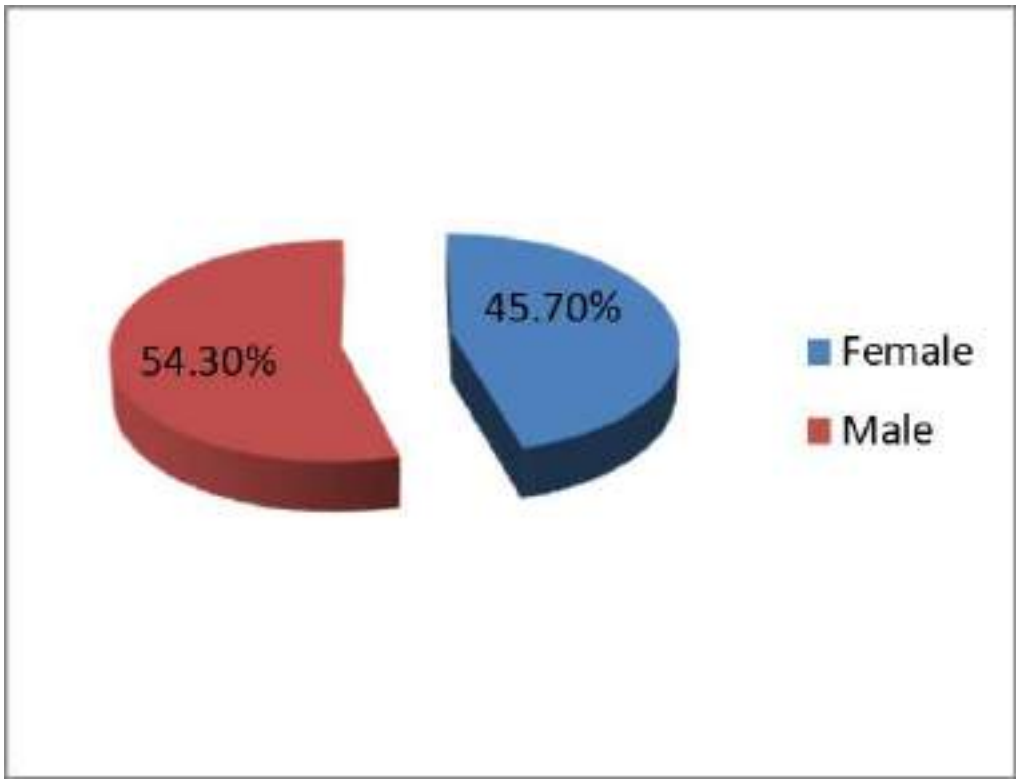

FIGURE 2: DISTRIBUTION OF PATIENTS ACCORDING TO GENDER

TABLE 4: DISTRIBUTION OF PATIENTS ACCORDING TO TYPE OF STROKE

Type of Stroke	No. of cases (n=116)	Percentage
Ischaemic	103	88.7%
Haemorrhagic	13	11.2%
Total	116	100.0%

In our study, 88.7% (103 patients) were diagnosed with ischaemic infarctions and 11.2% (13 patients) were diagnosed with primary haemorrhage.

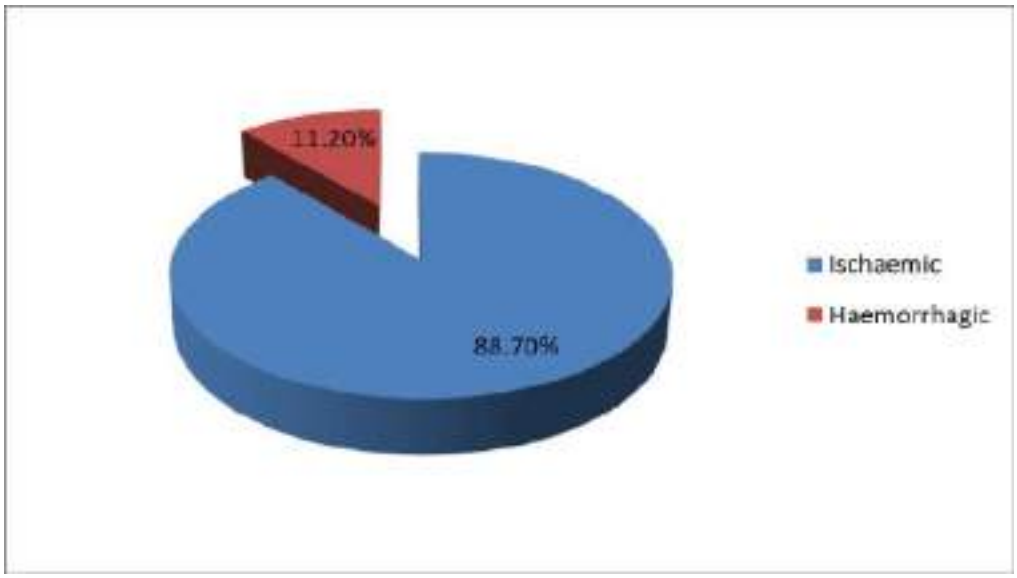

FIGURE 3: DISTRIBUTION OF PATIENTS ACCORDING TO TYPE OF STROKE

TABLE 5: DISTRIBUTION OF PATIENTS ACCORDING TO ASSOCIATED CO-MORBIDITIES

CO-MORBIDITY	No. of cases (n=116)	Percentage
Diabetes Mellitus	40	34.5%
Hypertension	68	58.6%
Coronary artery disease	36	31.0%
Dyslipidaemia	30	25.9%

In our study, 58.6% (68 patients) were hypertensives, 34.5% (40 patients) were diabetic. 31% (36 patients) had a past history of coronary artery disease while dyslipidaemia was present in 25.9% of the cases.

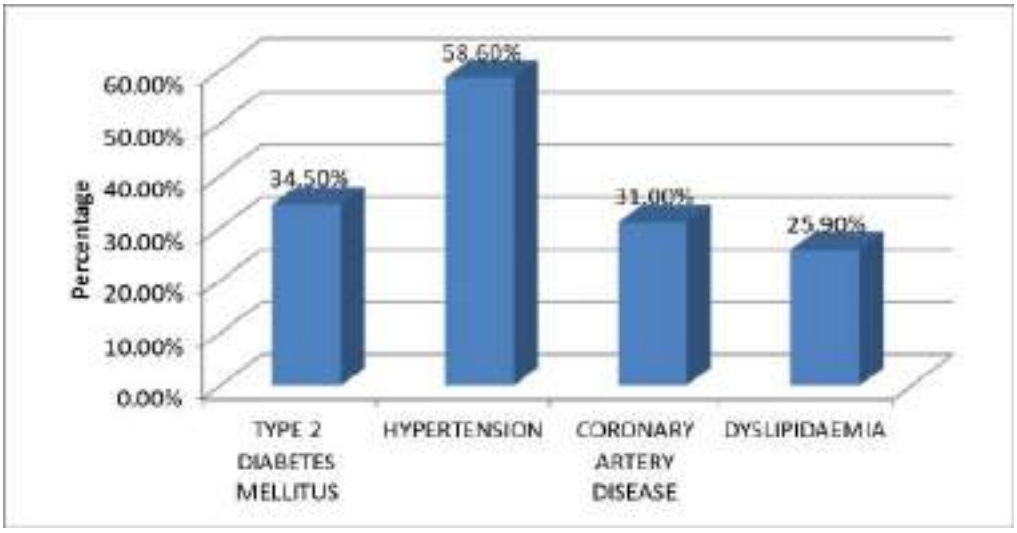

FIGURE 4: DISTRIBUTION OF PATIENTS ACCORDING TO ASSOCIATED CO-MORBIDITIES

TABLE 6: DISTRIBUTION OF PATIENTS ACCORDING TO BUN/CREATININE RATIO

BUN/Cr RATIO group	No. of cases (n=116)	Percentage
≤15	54	46.6%
> 15	62	53.4%
Total	116	100.0%

According to the blood urea nitrogen (BUN) to creatinine (Cr) ratio (BUN/Cr), patients were divided into dehydrated (BUN/ Cr > 15) and non-dehydrated (BUN/Cr ≤ 15) groups. In our study, 53.4% (62 patients) had BUN/Creatinine ratio >15 at the time of admission and 46.6% (54 patients) had BUN/Creatinine ratio ≤ 15 at the time of admission.

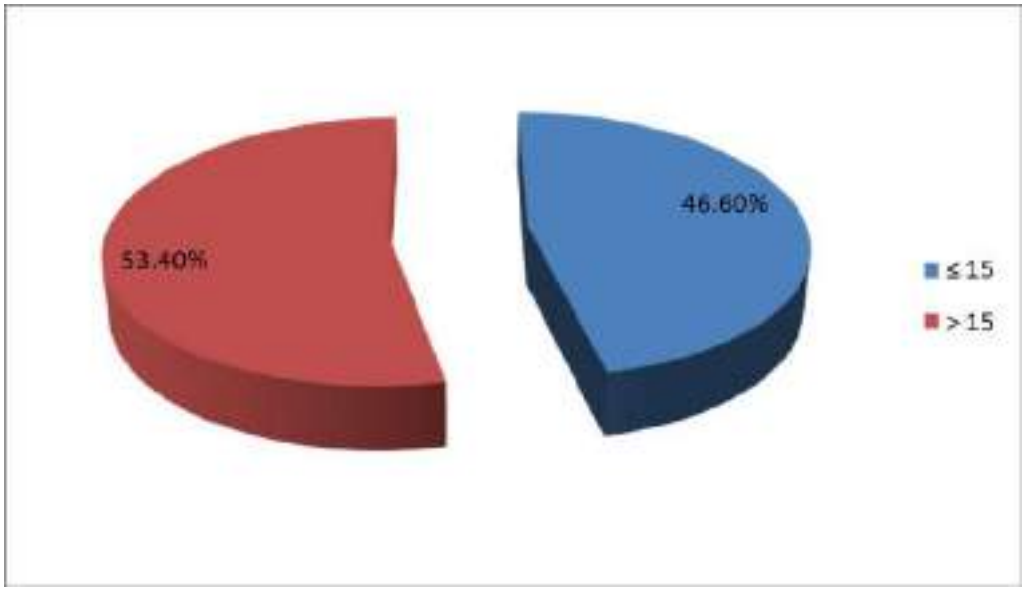

FIGURE 5: DISTRIBUTION OF PATIENTS ACCORDING TO BUN/CREATININE RATIO

ANALYZING THE COURSE OF HOSPITAL STAY OF ALL PATIENTS

TABLE 7A: ICU REQUIREMENT IN THE ADMITTED PATIENTS

ICU REQUIRED	No. of cases (n=116)	Percentage
No	59	50.9%
Yes	57	49.1%
Total	116	100.0%

In our study 49.1% (57 patients) needed ICU care while 50.9% (59 patients) were managed in the ward (as per the hospital protocol)

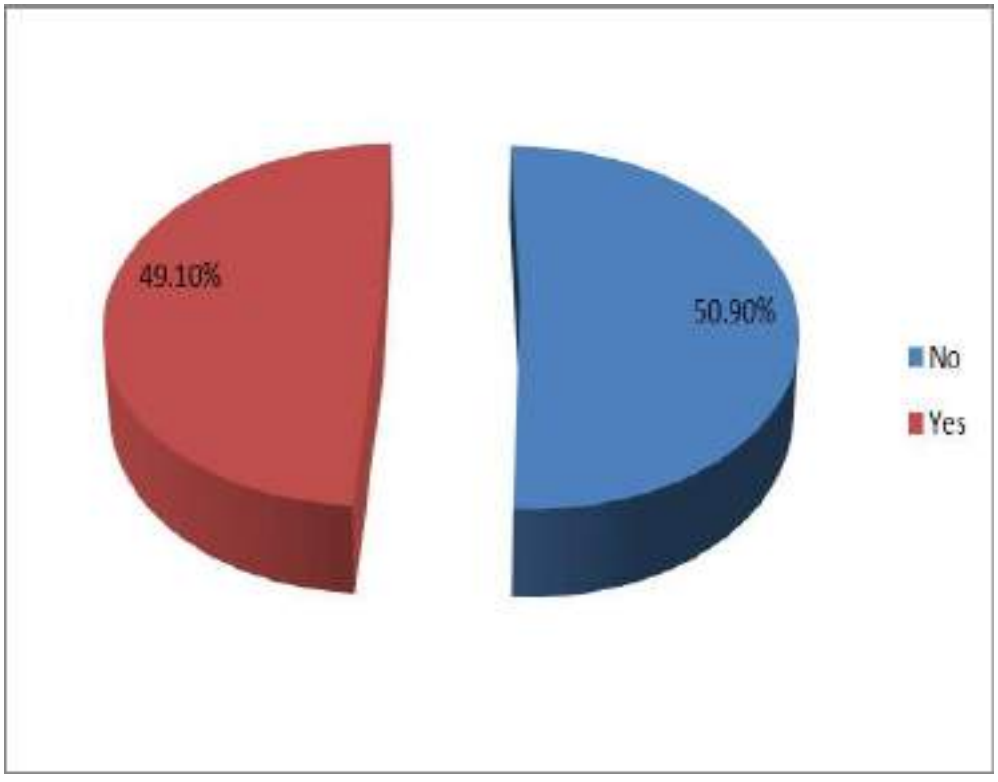

FIGURE 6A: ICU REQUIREMENT IN THE ADMITTED PATIENTS

TABLE 7B: MORTALITY RATE

		No. of cases (N=116)	Percentage
DEATH	No	106	91.4%
	Yes	10	8.6%
	Total	116	100.0%

In our study, there were 10 (8.6%) deaths.

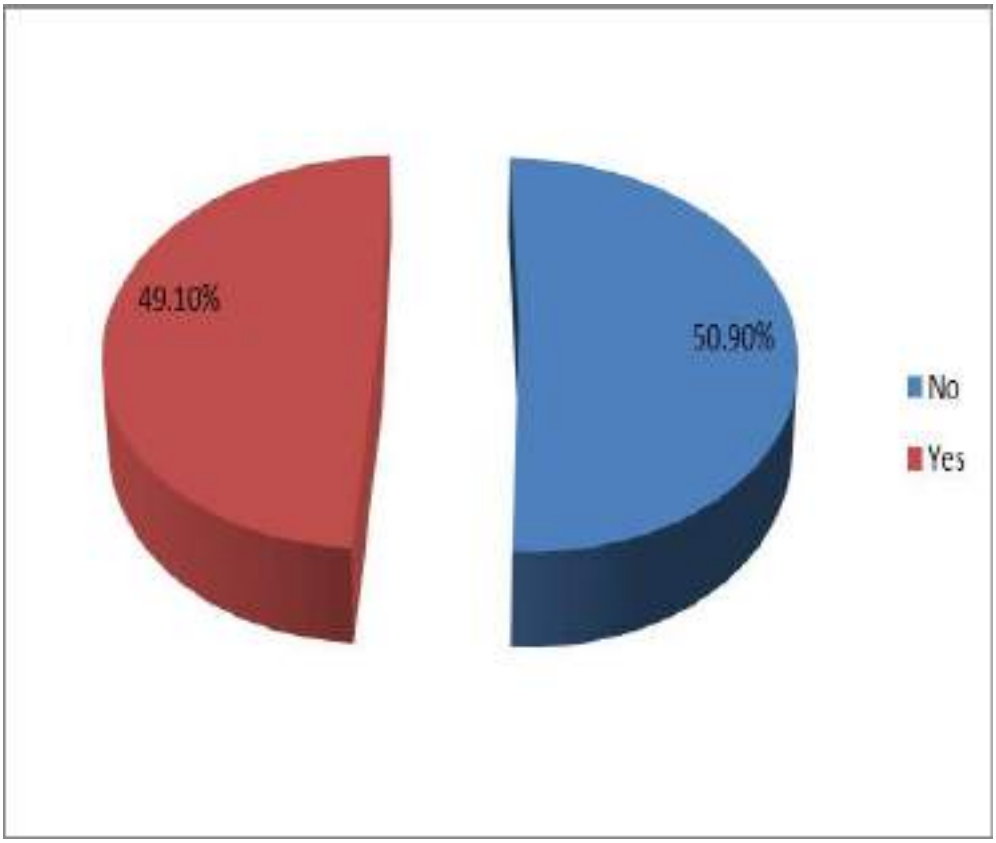

FIGURE 6B: MORTALITY RATE

TABLE 8: ANALYSIS OF DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS ENROLLED IN THE STUDY

	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	116	35.00	88.00	61.35	11.14
SBP (mmHg)	116	90.00	200.00	130.86	24.12
DBP (mmHg)	116	60.00	110.00	77.59	9.84
GCS on admission	116	3.00	15.00	11.85	3.37
NIHSS on admission	116	1.00	33.00	11.97	8.57
BUN/Creatinine Ratio	116	7.68	40.50	16.38	5.40
TC (mg/dl)	116	64.00	250.00	157.51	47.46
TG (mg/dl)	116	50.00	479.00	135.72	57.86
HDL (mg/dl)	116	22.00	72.00	36.33	8.02
LDL (mg/dl)	116	43.00	190.00	112.14	36.19
Urine specific gravity	116	1.01	1.03	1.02	0.01
Duration of stay in hospital (in days)	116	2.00	40.00	9.05	6.66
mRS grade Day 7 / Discharge	116	0.00	6.00	2.89	1.53
mRS grade Day 30	116	0.00	6.00	2.76	1.87

We analysed demographical, various clinical and biochemical parameters along with hospital course in patients admitted with stroke. A total of 116 patients with acute stroke participated in the study and poor outcome (dependency/death) was seen in 61 (52.6%) patients.

The present study shows mean age of presentation in stroke to be 61.35 (+/- 11.14) years. The neurological status of the patient and the severity of stroke were assessed by using the GCS and NIHSS scoring system. Outcome was assessed by mRS score at day 30. Patients were divided into 2 groups based on mRS score. The first group included patients with mRS score ≤ 2 on day 30 and the second group included those with mRS >2 on day 30. Demographic characteristics, clinical characteristics, NIHSS score (≥12 or <12), GCS score (≤12 or >12), BUN/Creatinine ratio (≤ 15 or >15) and other variables were compared between the 2 groups. We also analysed the different parameters of hospital course such as ICU requirement, duration of hospital stay and death.

TABLE 9: COMPARISON OF AGE GROUP WITH OUTCOME VARIABLE (mRS SCORE AT DAY 30)

		mRS day 30				Total	Chi-square value	p-value
		≤2		> 2				
Age group	< 40	3	5.5%	1	1.6%	4	13.353	0.004
	41-50	12	21.8%	4	6.6%	16		
	51-60	23	41.8%	18	29.5%	41		
	> 60	17	30.9%	38	62.3%	55		
Total		55	100.0%	61	100.0%	116		

In our study, majority patients 55 (47.4%) were more than 60 years of age. The mean age of presentation was 61.35 (+/- 11.14) years. In patients with poor outcome i.e., mRS >2 on day 30, 38 (62.3%) patients were above the age of 60 years, 18 (29.5%) patients belonged to age group 51 - 60 years, 4 (6.6%) patients belonged to age group 41-50 years and 1 (1.6%) patient below the age of 40 years. The mean age of the patients with poor outcome (mRs > 2) was 67 +/- 10.9 year as compared to 55 +/- 7.5 year in patients with good outcome (mRs ≤2). Our study shows that the patients with age more than 60 years were significantly associated with mRS >2 on day 30 as compared to other age groups and hence associated with poor outcome (dependency/death).

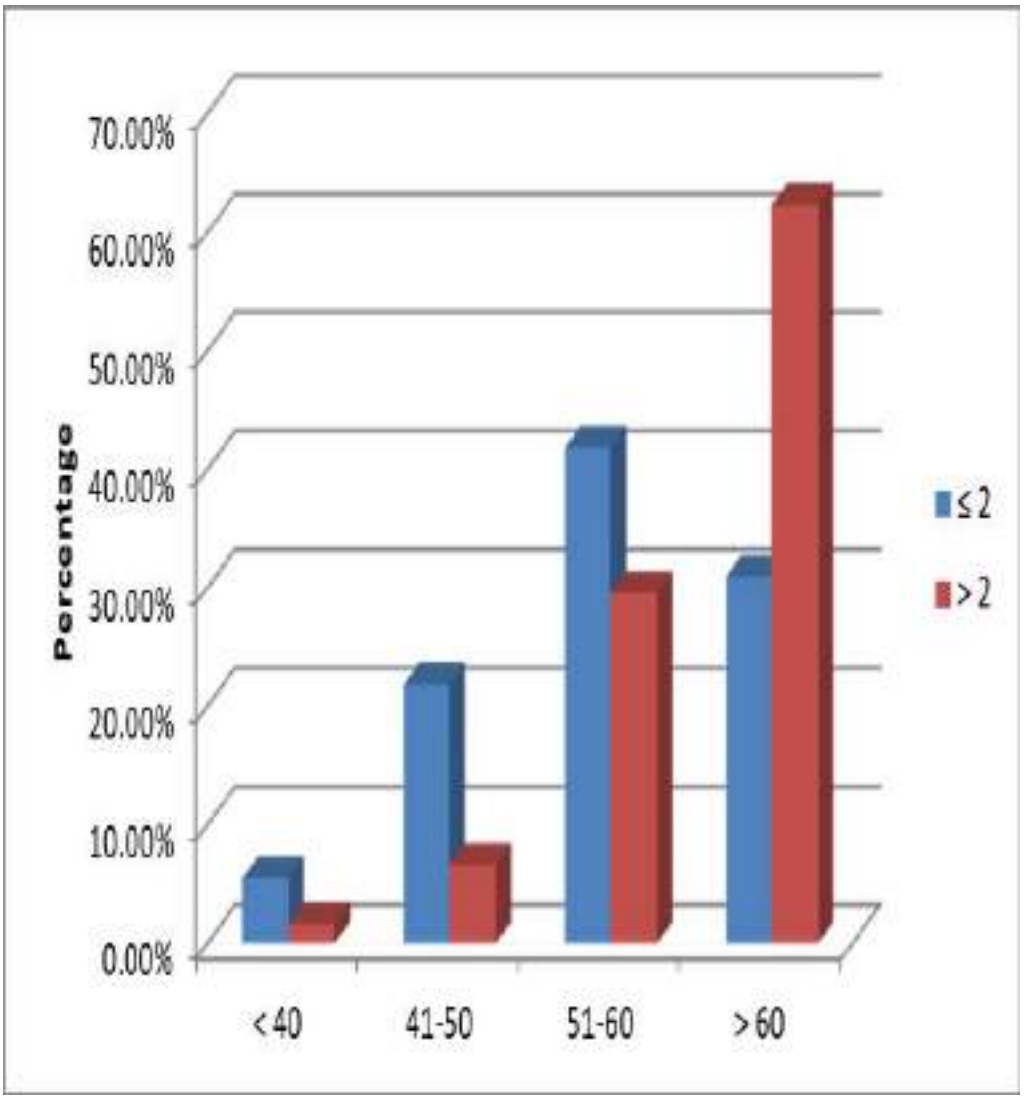

FIGURE 7: ASSOCIATION BETWEEN AGE GROUP AND mRS SCORE AT DAY 30

TABLE 10: COMPARISON OF GENDER WITH OUTCOME VARIABLE (mRS SCORE AT DAY 30)

		mRS day 30				Total	Chi-square value	p-value
		≤ 2		> 2				
Sex	F	30	54.5%	23	37.7%	53	3.306	0.093
	M	25	45.5%	38	62.3%	63		
Total		55	100.0%	61	100.0%	116		

In our study, 63 (54.3%) patients were males and 53 (45.7%) were females. Amongst patients with poor outcome i.e., mRS >2 on day 30, 38 (62.3%) patients were males and 23 (37.7%) patients were females. There was no statistically significant association of gender with outcome in our study.

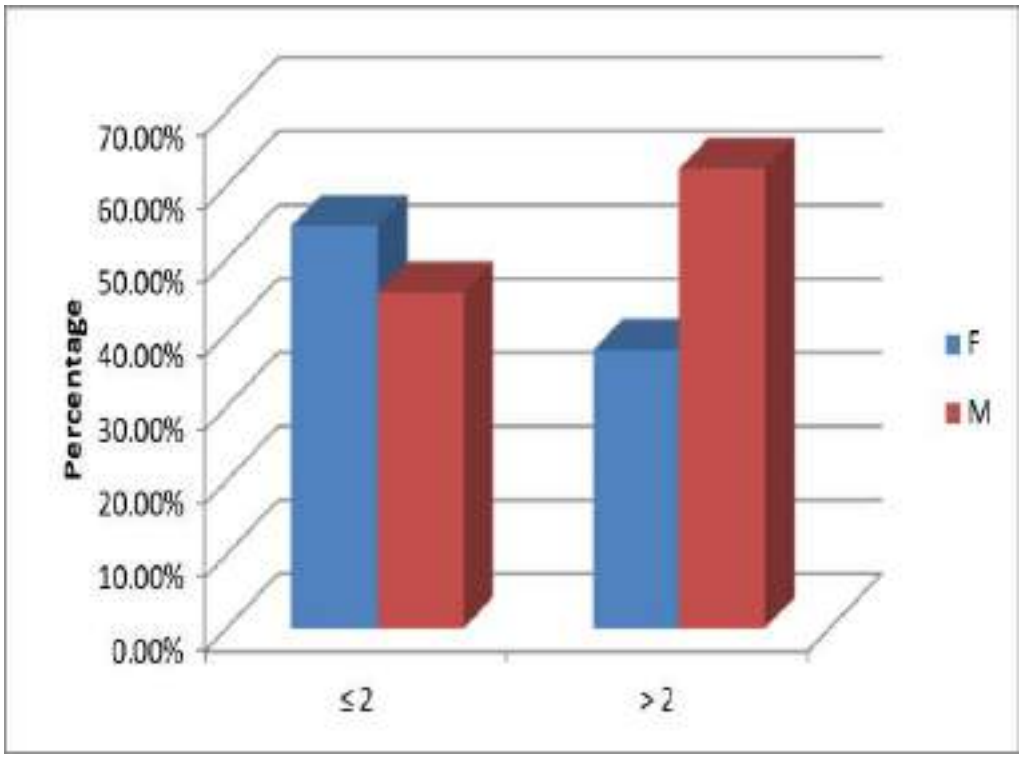

FIGURE 8: ASSOCIATION BETWEEN GENDER AND mRS SCORE AT DAY 30

TABLE 11: COMPARISON OF HOSPITAL COURSE PARAMETERS WITH OUTCOME VARIABLE (mRS SCORE AT DAY 30)

		mRS day 30				Total	Chi-square value	p-value
		≤ 2		> 2				
GCS Group	≤12	0	0.0%	61	100.0%	61	116.000	0.000
	> 12	55	100.0%	0	0.0%	55		
NIHSS Group	< 12	55	100.0%	0	0.0%	55	116.000	0.000
	≥12	0	0.0%	61	100.0%	61		
Type of Stroke	Ischemic	55	100.0%	48	78.7%	103	101.045	0.000
	Haemorrhagic	0	0.0%	13	21.3%	13		
ICU Required	No	55	100.0%	4	6.6%	59	101.045	0.000
	Yes	0	0.0%	57	93.4%	57		
Duration of Hospital Stay (in days)	≤10	54	98.2%	21	34.4%	75	51.445	0.000
	> 10	1	1.8%	40	65.6%	41		

We also analysed the different parameters of hospital course such as baseline GCS, NIHSS score at admission, ICU requirement, duration of hospital stay and death. On statistical analysis, all parameters were significantly associated with mRS score >2 (dependency/death) on day 30.

A higher stroke severity at admission, as measured by assessing NIHSS and GCS scores, was observed to have a significant association with mRS >2 on day 30 and was found to be a predictor of poor neurological outcome with disability or mortality. Patients with a NIHSS score ≥12 at admission were significantly associated with the dependency or mortality on day 30 as compared to patients with NIHSS score <12 ($p<0.001$). Similarly, patients with a GCS score ≤12 at admission were more likely to be associated with dependency or mortality on day 30 as compared to patients with GCS score >12 ($p<0.001$).

All the patients (100%, n=13) with haemorrhagic stroke had mRS score of >2 on day 30 while 46.6% (48 patients) of ischaemic stroke had mRS score of > 2 on day 30. Haemorrhagic stroke was found to have significant association with poor outcome in our study (p<0.001). In our study 49.1% (57 patients) needed ICU care and there were 10 (8.6%) deaths. The average duration of hospital stay was 9.05 days. Patients who had > 10 days of stay in hospital and those who required ICU care showed significant association with poor outcome on day 30.

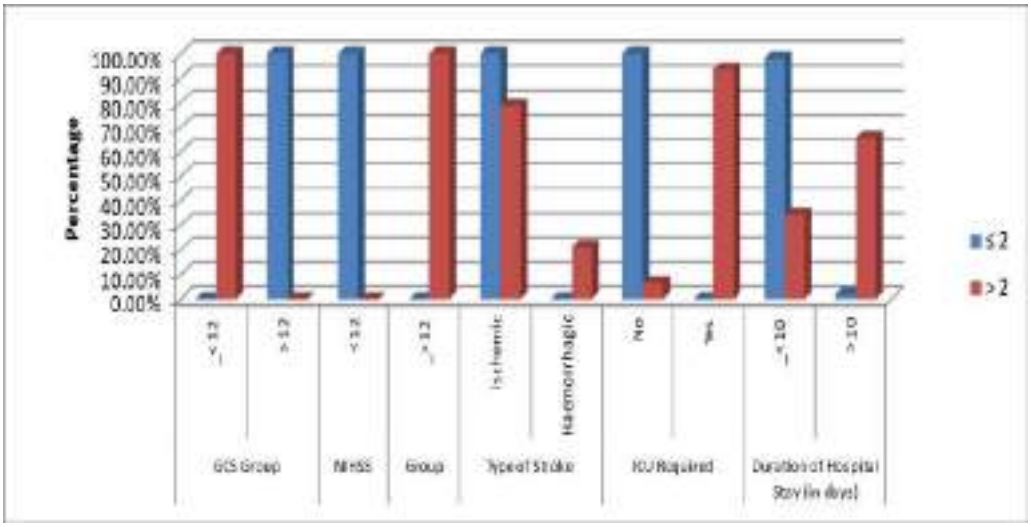

FIGURE 9: COMPARISON OF HOSPITAL COURSE PARAMETERS WITH mRS AT DAY 30

TABLE 12: COMPARISON OF BUN/Cr RATIO WITH OUTCOME VARIABLE (mRS SCORE AT DAY 30)

TYPE OF STROKE	BUN/Cr RATIO	mRS day 30				Total	Chi-square value	p-value
		≤ 2		> 2				
Ischaemic	≤15	38	79.2%	17	30.9%	55	23.986	0.000
	> 15	10	20.8%	38	69.1%	48		
Total		48	100.0%	55	100.0%	103		
Haemorrhagic	≤15	0	0.0%	5	38.5%	5		
	> 15	0	100.0%	8	61.5%	8		
Total		0	100.0%	13	100.0%	13		

In our study, 88.7% (103 patients) had ischaemic infarctions while 11.2% (13 patients) had haemorrhagic stroke. Of 103 patients with Ischaemic stroke, 53.4% (55 patients) were classified in the non-dehydrated subgroup while 46.6% (48 patients) in the dehydrated subgroup. 69.1% (38 patients) of ischaemic stroke with admission dehydration had poor outcome on day 30 (dependency/death) while 30.9% (17 patients) of ischaemic stroke in the non-dehydrated subgroup had poor outcome on day 30. In our study, BUN/Creatinine ratio > 15 had significantly higher association with mRS score >2 on day 30 in ischaemic stroke and hence associated with poor outcome (dependency/death) in patients with ischaemic stroke. No such association with observed in patients of haemorrhagic stroke.

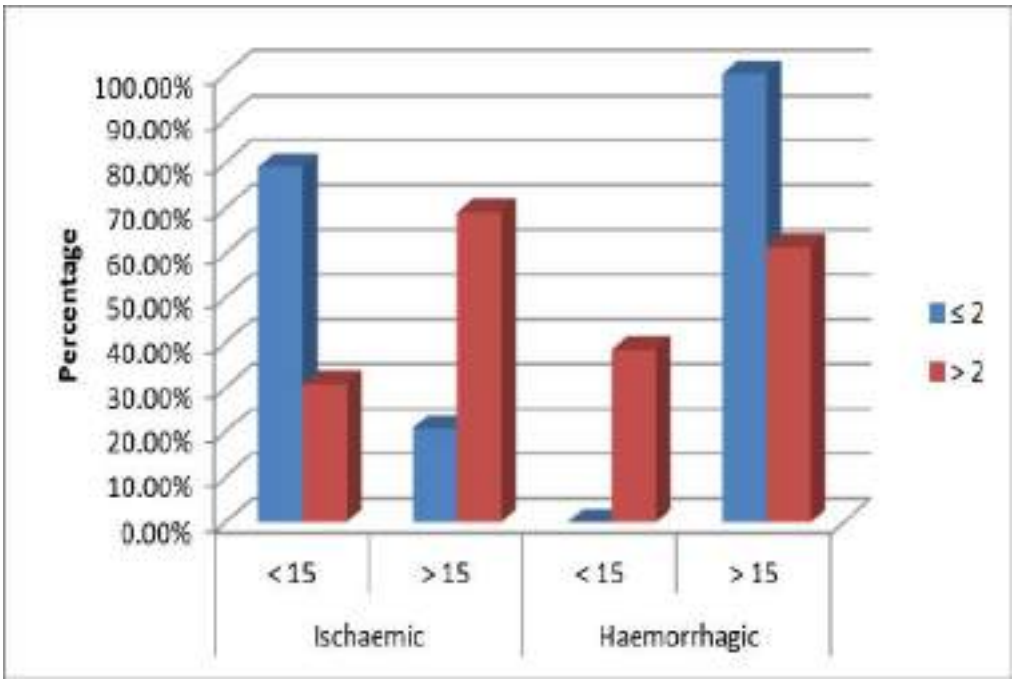

FIGURE 10: COMPARISON OF BUN/Cr RATIO WITH mRS SCORE AT DAY 30

TABLE 13: ANALYSIS OF PATIENT CHARACTERISTICS IN BUN/Cr RATIO SUBGROUPS

		BUN/Cr				Total	Chi-square value	p-value
		≤ 15 (Non-dehydrated)		>15 (Dehydrated)				
Age group	1	2	3.7%	2	3.2%	4	3.005	0.391
	2	9	16.7%	7	11.3%	16		
	3	22	40.7%	19	30.6%	41		
	4	21	38.9%	34	54.8%	55		
Sex	F	26	48.1%	27	43.5%	53	0.325	0.620
	M	28	51.9%	35	56.5%	63		
GCS	≤12	16	29.6%	45	72.6%	61	21.335	0.000
	> 12	38	70.4%	17	27.4%	55		
NIHSS	< 12	38	70.4%	17	27.4%	55	21.355	0.000
	≥12	16	29.6%	45	72.6%	61		
Diabetes mellitus	N	43	79.6%	32	51.6%	75	9.914	0.002
	Y	11	20.4%	30	48.4%	41		
Hypertension	N	23	42.6%	25	40.3%	48	1.004	0.605
	Y	31	57.4%	37	59.7%	68		
CAD	N	44	81.5%	36	58.1%	80	7.395	0.009
	Y	10	18.5%	26	41.9%	36		
Dyslipidaemia	N	42	77.8%	44	71.0%	86	0.698	0.403
	Y	12	22.2%	18	29.0%	30		
Pre-existing diuretic t/t	N	45	83.3%	42	67.7%	87	3.742	0.057
	Y	9	16.7%	20	32.3%	29		
H/o any addiction	N	35	64.8%	41	66.1%	76	0.022	0.882
	Y	19	35.2%	21	33.9%	40		
Urine specific gravity	< 1.010	51	94.4%	11	17.7%	62	68.246	0.000
	> 1.010	3	5.6%	51	82.3%	54		
Hospital Stay	≤10	43	79.6%	32	51.6%	75	9.914	0.002
	> 10	11	20.4%	30	48.4%	41		

ICU requirement	N	39	72.2%	20	32.3%	59	18.440	0.000
	Y	15	27.8%	42	67.7%	57		
mRS day 30	≤2	38	70.4%	17	27.4%	55	21.355	0.000
	>2	16	29.6%	45	72.6%	61		
Total		54	100.0%	62	100.0%	116		

In our study of 116 patients, 46.6% (54 patients) were classified in the non-dehydrated subgroup while 53.4% (62 patients) in the dehydrated subgroup. 54.8% (34 patients) in the dehydrated subgroup were more than 60 years of age. The mean age of onset in dehydrated subgroup was 64.4 (+/- 12.15) year and in non-dehydrated subgroup was 57.9 (+/- 8.7) year. Compared with the non-dehydrated subgroup, patients with dehydration status had higher frequency of diabetes mellitus (48.4% vs 20.4%, p=0.002) and coronary artery disease (41.9% vs 18.5%, p=0.009), worse median NIHSS and GCS score at admission and higher urine specific gravity (n=51, 82.3%, p<0.001). Previous history of diuretic treatment was present in 32.3% (20 patients) in dehydrated subgroup. No statistically significant influence of diuretic use was observed on the dehydration status of patient (p=0.057). Patients in the dehydrated subgroup also showed longer length of hospital stay (p=0.002), more ICU requirement (p<0.001) and worse outcome mRS score at day 30 (p<0.001).

TABLE 14: ASSOCIATION OF INDEPENDENT VARIABLE WITH mRS SCORE AT DAY 30 – UNIVARIATE ANALYSIS

		mRS day 30				Chi-square value/t	p-value
		≤ 2		> 2			
Age group	< 40	3	5.5%	1	1.6%	13.353	0.004
	41-50	12	21.8%	4	6.6%		
	51-60	23	41.8%	18	29.5%		
	> 60	17	30.9%	38	62.3%		
Gender	F	30	54.5%	23	37.7%	3.306	0.093
	M	25	45.5%	38	62.3%		
Type of Stroke	Ischemic	55	100.0%	48	78.7%	101.045	0.000
	Haemorrhagic	0	0.0%	13	21.3%		
GCS	≤ 12	0	0.0%	61	100.0%	116.000	0.000
	> 12	55	100.0%	0	0.0%		
NIHSS	< 12	55	100.0%	0	0.0%	116.000	0.000
	≥ 12	0	0.0%	61	100.0%		
Diabetes Mellitus	N	37	67.3%	39	63.9%	0.143	0.706
	Y	18	32.7%	22	36.1%		
Hypertension	N	25	45.5%	23	37.7%	0.716	0.397
	Y	30	54.5%	38	62.3%		
CAD	N	39	70.9%	41	67.2%	0.185	0.667
	Y	16	29.1%	20	32.8%		
Dyslipidaemia	N	37	67.3%	49	80.3%	2.571	0.109
	Y	18	32.7%	12	19.7%		
BUN/Cr group	≤ 15	38	69.1%	16	26.2%	21.355	0.000
	> 15	17	30.9%	45	73.8%		
Urine specific gravity group	< 1.010	36	65.5%	26	42.6%	6.060	0.016
	> 1.010	19	34.5%	35	57.4%		
Hospital Stay	≤ 10	54	98.2%	21	34.4%	51.445	0.000
	> 10	1	1.8%	40	65.6%		

In our study, at the time of admission various clinical and biochemical parameters along with stroke severity were evaluated and their association was seen with the outcome i.e., dependency or mortality on day 30. It was seen that the age more than 60 years had a significant association with the dependency or mortality on day 30 and hence associated with poor outcome. Gender did not show any significant association with the disability on day 30. Detailed history taking revealed the presence of various risk factors like hypertension (n=68), diabetes (n=40), coronary artery disease (n=36) and dyslipidaemia (n=30) in the study population. However, no statistically significant association was seen between the various risk factors and the outcome. An increased stroke severity at presentation, as assessed by NIHSS and GCS scores, was significantly associated with poor outcome (dependency or mortality). Haemorrhagic stroke was found to have significant association with poor outcome in our study ($p<0.001$). BUN/creatinine ratio was assessed at the time of admission. A significantly higher proportion of patients with dependency or mortality (n=45, 73.2%) had BUN/Creatinine >15 as compared to patients without disability (n=17, 30.9%). Admission dehydration was found as an independent factor predictive of poor outcome in patients with Ischaemic stroke. No statistically significant association was seen between the BUN/Creatinine ratio and the outcome in patients of haemorrhagic stroke. A significant association was seen between Urine specific gravity > 1.010 and poor outcome ($p<0.016$), as (n=35, 57.4%) of patients with poor outcome had a Urine specific gravity > 1.010 as compared to 19 (35.4%) patients with good outcome. Patients who had > 10 days stay in hospital and those who required ICU care showed significant association with poor outcome on day 30.

TABLE 15: MULTIVARIATE ADJUSTED ANALYSIS OF SIGNIFICANT FACTORS FOR PREDICTING OUTCOME IN PATIENTS WITH STROKE

	p-value	Exp(B)	95% C.I.for EXP(B)	
			Lower	Upper
BUN/Cr Ratio > 15	0.004	63.45	3.78	1064.12
Urine specific gravity > 1.010	0.058	0.07	0.00	1.10
Hospital Stay > 10	0.000	147.75	13.79	1583.32

On multivariate adjusted analysis, BUN/creatinine >15 and hospital stay > 10 days were found to be independent predictor of poor outcome.

DISCUSSION

Stroke accounts for almost 5% of all disability-adjusted life-years and 10% of all deaths worldwide, with the bulk of this burden (>75% of deaths from stroke and >80% of disability-adjusted life-years) occurring in low-income and middle-income countries.[3] Several factors have been reported to predict the outcome of acute stroke, such as age and gender, stroke severity at presentation or high initial National Institute of Health Stroke Scale (NIHSS) score, total anterior circulation involvement in the brain, infarction volume, history of diabetes mellitus, in-hospital infection, length of hospital stay and dehydration.[29]

Hydration status at the time of stroke has been acknowledged as an important determinant in early stroke recovery and outcome factor. A study by Rodriguez et al[13] have observed that the elderly patients presenting with transient ischaemic attack or acute ischaemic stroke often demonstrate increased plasma osmolality, likely representing a volume depleted state, and possibly contributes to worsening cerebral ischaemia and poor neurological outcome. The role of volume depletion as a risk factor for poor outcome was further studied by Lin et al[14] who demonstrated that blood urea nitrogen/ creatinine (BUN/Cr) ratio higher than 15 was more frequently seen in SIE (Stroke in Evolution) patients. The present study was designed to determine the association between BUN/Creatinine ratio, which is a marker of relative dehydration and the outcome in acute stroke.

A total of 116 patients who were admitted in DMC&H with the diagnosis of stroke were included in the study. We analyzed demographical, various clinical and laboratory parameters along with stroke severity. The outcome parameters used in our study was defined by the course in hospital (ICU requirement, duration of hospital stay) and mRS score at 1 month. Good outcome was defined by patients having mRS score of ≤ 2 (though they had some disability but were still independent in their activities) and poor outcome when the mRS score was > 2 (suggesting dependency or death).

The present study on univariate analysis, showed mean age of presentation in stroke to be 61.35 (+/-11.14) years and this was in accordance to the previous studies by Bhatia K et al[15] (57.17 +/- 10.25 years) and Wang et al[36] (56.3 +/- 11.20 years). The age distribution in our study showed that 47.4% of the patients were more than 60 years of age, while 35.3% of the patients belonged to the age group between 51 to 60 years and 13.8% patients belonged to age group between 41 to 50 years. Majority of patients in our study were older and had age more than 50 years. The study done by Bruce Ovbiagele et al[4] also reported that the incidence of stroke doubles for every successive decade after the age of 55 years. This data is also consistent with a previous study done by Chong J et al[37] with majority of patients (n=684, 70%) belonging to the age group between 50-79 years. In our study, age more than 60 years was significantly associated with poor outcome (p=0.004). Age as a predictor of poor outcome was in accordance with various previous studies by Schrock JW et al[9], Elena et al[38] and Nakayama H et al[39]. However, studies by Kwan J et al[7] and Bhatia K et al[15] did not observed significant association of age with stroke outcome.

Our study had males (54.3%) more as compared to females (45.7%) which was in accordance with other previous studies by Reeves et al[40] and Haast et al[41], which also reported that the chances of stroke rates are higher in men than women. The Oxford Vascular Study also showed lower ischaemic stroke incidence for women than men aged 55–74 years, but incidence increased in women aged 85 years and older.[42] Similar results were seen in a 56-year follow-up prospective study from the Framingham Heart Study including 10,076 participants that women had a higher stroke incidence above 85 years of age, lower at all other ages.[43] The study done by T B Wyller also reported that the prevalence of stroke is higher among men up to the age of approximately 80 years, after which it becomes higher in women.[44] Part of this can be explained by a lower global life expectancy for men versus women from 85 years: 5.9 versus 6.8 years, respectively. Also,

women experience stroke later than men potentially because of loss of protection by estrogen after menopause, as seen with other cardiovascular risk factors.

Female gender was reported as an independent predictor of poor prognosis in studies by Appelros P et al[45] and Di Carlo A et al[46]. However, no statistically significant association of gender with the outcome was observed in our study on univariate analysis and the finding was similar to results seen in previous studies by Kwan J et al[7], Schrock JW et al[9] and Bhatia k et al[15]. Various other studies done by Lin LC et al[14], Mizrahi et al[47] had also shown similar results.

In our study, 88.7% had ischaemic stroke while 11.2% had haemorrhagic stroke. Higher incidence of ischaemic stroke was in accordance with the various previous studies by Bruce Ovbiagele et al[4], Chong J et al[37] and Haast et al[41]. Haemorrhagic stroke was found to have significant association with poor outcome (dependency/ death) in our study ($p<0.001$). Similar results were seen in study done by Andersen et al[48] who reported that the haemorrhagic stroke is significantly associated with a higher risk of death than ischaemic stroke, even after adjustment for age, sex, initial stroke severity, and relevant cardiovascular risk factors. Similarly, in a study done by David et al[49], haemorrhagic stroke was found to be an independent predictor of poor neurologic outcome, nearly doubling the odds of long-term disability.

On assessing co-morbid conditions, hypertension was noted in majority of the patients (58.6%) followed by diabetes mellitus in 34.5% of the cases, coronary artery disease in 31% of the cases while dyslipidaemia was present in 25.9% of the cases. These co-morbid conditions were comparable to other studies done by Bhatia K et al[15] and Amelia K et al[50]. However, no statistically significant association was found between the presence of various risk factors and the outcome parameter in our study. Similar results were seen in previous studies by Kwan J et al[7] and Bhatia K et al[15] .

The neurological status of the patient and the severity of stroke were assessed by using the NIHSS and GCS scores. A higher percentage of patients with poor outcome had a higher initial NIHSS score (12 or more) than the patients with good outcome, which was statistically significant ($p<0.001$). Similarly, patients with a GCS score ≤12 at admission were also more likely to be associated with dependency or mortality on day 30 as compared to patients with GCS score >12 ($p<0.001$). A higher stroke severity at admission, as assessed by NIHSS and GCS score was observed to be a significant risk factor for poor outcome at one month. Similar results were seen in various studies by Kwan J et al[7], Lin LC et al[14] and Bhatia K et al[15]. The study done by Schrock JW et al[9] also found higher NIHSS score at time of presentation of stroke as an independent predictor of poor outcome.

We analysed various parameters of hospital course such as duration of hospital stay, ICU requirement and mortality. In our study, the average duration of hospital stay was 9.05 (+/- 6.66) days, 49.1% required ICU care and mortality rate was 8.6%. Patients who had prolonged hospital stay (> 10 days) and those who required ICU care had significant association with poor outcome (dependency or death) on day 30. Our findings were in accordance with the previous studies by Tirschwell DL et al[51] and Spratt N et al[52]. The study done by Rockwood K et al[53] observed that the patients in whom hospital stay was longer tends to be older, have delirium or dementia and are required to transfer to long term care (LTC) institutions, and/or remain dependent in essential activities of daily living. Similar results were seen in a study done by Michelle et al[54] in which a longer LOS (length of stay) showed a negative association with discharge to community for both mild and moderately impaired patients.

A significantly higher proportion of patients with dependency or mortality (n=45, 73.2%) had BUN/Creatinine >15 as compared to patients without disability (n=17, 30.9%). In our study BUN/Creatinine >15, a marker of relative dehydration was significantly associated with

poor outcome (dependency/death). This was similar to results noted in previous studies done by Schrock JW et al[9], Lin LC et al[14], Bhatia K et al[15], Dehghani Firoozabadi M et al[25] and Elena et al[38]. Similarly, in a study done by Bahouth MN et al[24] , volume contracted state (VCS) at the time of stroke was associated with an increased odds of worse short-term outcome even after adjustment for other confounders and markers of stroke severity (e.g., infarct size). VCS was defined via surrogate markers (blood urea nitrogen/creatinine ratio >15 and urine specific gravity >1.010). However, it was not in accordance with a previous study done by Bahrainwala Z et al[28], in which elevated BUN/creatinine ratio was associated with an increased odds of severe hemispatial neglect in unadjusted models (OR = 4.1; 95% CI, 1.2, 14.4), but there was loss of significance in adjusted models (OR = 4.43; 95% CI, 0.99, 19.8) after adjustment for age, infarct volume, sex, and NIHSS score.

In our study, admission dehydration as defined by BUN/creatinine > 15 was significantly associated with poor outcome in ischaemic stroke but this dehydration marker showed no association in patients with haemorrhagic stroke. Similar results were seen in study done by Liu CH et al[27] in which acute ischaemic stroke with admission dehydration (BUN/ Cr > 15) was found to have significant association with longer length of hospital stay, worse Barthel index (BI) and higher mRS score at discharge and higher mortality rates than those without dehydration (BUN/Cr < 15). Also, acute haemorrhagic stroke with or without presence of dehydration at the time of admission did not showed any difference in length of hospital stay and discharge outcomes in their study. In contrast to above, the study done by Lehmann et al[55] reported admission dehydration status as a significant and independent predictor of short-term mortality in patients of spontaneous, non-traumatic ICH ($p < 0.001$, OR 3.9, 95% CI 2.2–6.8).

We also compared the BUN/Creatinine subgroups, and noted that patients with BUN/Cr > 15 had older age (64.4 +/- 12.15 vs. 57.9 +/- 8.7 years), higher frequency of diabetes mellitus and coronary artery

disease, worse median NIHSS and GCS score at admission and higher urine specific gravity. In this group severity of stroke was more along with comorbid conditions hence, had longer length of hospital stay, more ICU requirement and subsequently worse outcome mRS score at 30 days which may be related to their dehydrated state. These findings were consistent with previous studies done by Liu CH et al[27], Rowat A et al[29] and Elena et al[38]. A prospective study was done by Lin et al[56] with aim to determine the effect of BUN/Cr based hydration therapy on rate of poststroke infection and length of stay (LOS) in acute ischemic stroke. The hydration group had a significantly lower poststroke infection rate than did the control group (7.5% versus 17.5%, p = .018) and hence, had a significantly shorter LOS (13.5 ± 11.6 versus 19.6 ± 14.6 days, p< .01).

In addition, we did not find any statistically significant association between use of diuretics and the BUN/Cr ratio in stroke patients. There is also suggestion and evidence from previous studies done by Elena et al[38] and Lehmann et al[55]. However, the findings were not consistent with a previous study done by Rodriguez GJ et al[13] in which patients of cerebral ischemic events with diuretics use had significantly higher mean plasma osmolality, a marker of relative dehydration or volume depletion compared with patients not taking diuretics (296.0 ± 8.0 vs. 292.4 ± 8.0 mOsm/kg, p = 0.0026).

The factors which had significant association with mRS score at day 30 on univariate analysis, were again analysed by multivariate analysis after removing the confounding factors. On multivariate analysis, only BUN/creatinine > 15 (p=0.004; exp B 63.4) and hospital stay > 10 days (p=0.000; exp B 147.7) were observed as independent predictors of poor outcome in acute stroke.

As BUN/creatinine >15 is considered to be indicative of relative dehydration, our findings support the role of volume depletion or relative dehydration as a risk factor predictive of poor outcome. Dehydration is known to cause increased blood viscosity, reduced

cardiac stroke volume, decreased blood pressure, impaired collateral flow and reduced cerebral perfusion, the factors that may worsen the effects of brain ischemia, resulting in greater brain damage, and more severe symptoms. Dehydration has also been shown to be associated with recurrent embolic stroke and thrombotic events including both arterial and venous in patients who had associated co-morbid conditions especially, hypertension, diabetes mellitus and coronary artery disease. That may be the reason for BUN/Cr as an independent predictor of poor outcome in acute stroke.

Although Urine specific gravity is also an indicator of hydration status of a patient, we did not observe urine specific gravity >1.010 as an independent risk factor for poor outcome (p=0.058) on multivariate adjusted analysis. Similar results were seen in previous studies by Bhatia K et al[15] and Bahouth MN et al[24]. This may be explained by the fact that the change in urine specific gravity does not always precede a change in BUN/creatinine ratio, thereby indicating that urine specific gravity may not be a warning sign for dehydration always. Also, the use of urine dipsticks for measuring urine specific gravity may not be a very reliable method. In a pilot study done by Rowat et al[57], urine dipstick underestimated urine specific gravity as compared to refractometry in acute stroke patients.

Our study had few limitations, first is the small sample size though we included both ischaemic and haemorrhagic strokes. We assessed short time outcome at 30 days. Though contribution of other factors like age, presence of comorbid conditions and previous stroke cannot be completely negated in the present study.

This study strengthens the existing evidence regarding the association of hydration status of patients who present with acute stroke to the emergency. Monitoring of the BUN/Creatinine needs to be emphasized in the management of acute stroke patients apart from using antiplatelet or antihypertensive drugs. The use of BUN/ Creatinine >15 as a marker of relative dehydration, can be helpful in detecting patients

with dehydration early and may play a role in preventing further deterioration in their neurological state, also reducing the stay in the hospital and improving their outcome.

SUMMARY AND CONCLUSION

- Stroke is a major cause of long-term disability among patients and has enormous emotional and socioeconomic consequences. During the early stroke recovery period, autoregulatory systems are impaired, leaving the brain vulnerable to blood viscosity and pressure changes that could further injure the area already compromised by decreased oxygen and nutrients.
- Over a period of one year, 116 patients admitted with stroke were studied. Majority of patients (47.4%) were older and had age more than 60 years.
- The mean age of presentation was 61.35 +/- 11.14 years with males (54.3%) were more as compared to females (45.7%).
- The present study showed higher incidence of ischaemic stroke (88.7%).
- Hypertension was noted as a risk factor in majority (58.6%) followed by diabetes mellitus in 34.5% of the cases, coronary artery disease in 31% of the cases while dyslipidaemia was present in 25.9% of the cases.
- Disability (mRS score at day 30 >2) was found to be present in 52.6% of the cases and mortality rate was 8.6%.
- The variables associated with poor outcome (mRS score at day 30 >2) were identified to be - (by univariate analysis): age > 60 years, baseline GCS ≤12, NIHSS ≥12 at admission, haemorrhagic stroke, prolonged hospital-stay (>10 days), BUN/creatinine >15 and urine specific gravity > 1.010.
- By multivariate analysis, BUN/creatinine >15 and longer hospital stay (> 10 days) were found to be independent predictor of poor outcome.
- Compared with the non-dehydrated subgroup, patients with dehydration status i.e., BUN/creatinine >15 were older (64.4 +/- 12.15 vs. 57.9 +/- 8.7 years), had higher frequency of diabetes mellitus (48.4% vs 20.4%) and coronary artery disease (41.9% vs 18.5%), worse median NIHSS and GCS score at admission, had

longer length of hospital stay, more ICU requirement and worse outcome mRS score at 30 days.

- Acute ischaemic stroke with admission dehydration (defined by BUN/creatinine >15) showed worse outcome mRS score at 30 days while no such association was seen in acute haemorrhagic stroke ($p<0.001$).

In conclusion, our study strengthens the existing evidence regarding the association of hydration status of patients who present with acute stroke to the emergency. Hence, monitoring of the BUN/creatinine ratio needs to be emphasized in the management of acute stroke patients apart from using antiplatelet or antihypertensive drugs.

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S NO	NAME	MRD NO	AGE	SEX				CO-MORBIDITIES AND PAST HISTORY					
					BLOOD PRESSURE	GCS	NIH STROKE SCALE	TYPE 2 DIABETES MELLITUS	HYPERTENSION	CORONARY ARTERY DISEASE	DYSLIPIDAEMIA	DIURETICS USE IN LAST 7 DAYS	H/O ANY ADDICTION
1	BS	941775	70	M	140/80	11	18	Y	N	Y	Y	Y	N
2	VK	940697	59	F	150/80	11	16	Y	N	N	Y	N	N
3	KC	942829	57	M	120/80	15	2	Y	Y	N	Y	N	Y
4	JS	954190	72	M	90/60	3	33	Y	N	N	Y	N	Y
5	BM	952671	72	M	110/70	7	20	N	N	Y	N	Y	Y
6	HS	938070	68	F	150/80	15	3	Y	Y	N	N	N	N
7	DM	936803	58	F	110/70	15	4	Y	Y	N	Y	N	N
8	NS	934663	58	M	110/70	11	20	N	N	N	N	N	Y
9	MS	934975	86	M	90/60	4	31	Y	N	Y	Y	Y	N
10	ML	933104	65	M	150/80	15	2	Y	Y	Y	N	Y	Y
11	PL	929801	70	F	160/80	7	29	N	N	Y	N	N	N
12	HS	924802	62	M	140/80	15	2	Y	N	N	Y	N	Y
13	BK	930468	63	F	120/80	15	6	Y	Y	Y	N	Y	Y
14	SB	896375	64	F	120/80	15	6	N	N	Y	N	Y	N
15	GK	927147	74	F	120/80	7	18	N	N	Y	Y	Y	N
16	SS	917386	38	M	160/90	15	2	N	Y	N	N	N	Y
17	K	660910	58	F	120/70	10	13	Y	N	Y	Y	N	N
18	HS	939328	70	F	140/80	7	22	Y	N	Y	Y	Y	N
19	KS	940279	72	M	90/60	3	31	N	N	Y	N	N	Y
20	RS	7181	62	M	110/70	15	2	N	N	N	N	N	Y
21	JS	951217	59	M	110/70	11	17	Y	N	N	N	N	Y
22	JK	951346	62	F	140/70	15	2	N	Y	N	N	N	N
23	SM	946606	65	M	140/80	7	19	Y	N	Y	N	N	Y
24	MK	944978	62	F	90/60	7	20	Y	N	N	Y	N	N
25	MS	949908	50	M	90/60	7	21	Y	Y	N	Y	N	Y
26	MK	956789	62	F	110/70	15	3	Y	Y	Y	Y	Y	N
27	GK	947032	62	M	110/70	15	5	N	Y	Y	N	Y	Y
28	HS	944584	48	F	110/70	15	4	N	N	N	N	N	N
29	KS	947479	62	M	120/80	15	5	Y	Y	N	N	N	Y
30	MS	946515	80	F	90/60	7	21	N	Y	Y	N	N	N
31	ZS	949362	50	M	120/80	15	2	Y	N	N	Y	N	Y
32	AK	948430	60	M	140/80	10	16	N	N	N	N	N	N
33	NS	924507	58	F	200/110	15	4	Y	Y	N	Y	N	N
34	MK	924821	46	F	170/90	15	2	N	Y	N	Y	N	N
35	PN	914419	72	M	130/80	11	13	N	Y	N	N	N	N
36	NS	926162	75	F	110/70	11	13	N	Y	N	N	N	N
37	KC	921305	80	M	130/80	11	16	N	N	Y	N	Y	N
38	RS	411760	50	M	120/80	15	5	N	N	N	Y	N	Y
39	MS	881010	72	M	150/90	11	18	N	Y	Y	N	Y	Y
40	RK	892180	62	F	110/70	15	6	N	N	Y	N	Y	N
41	KT	57652	85	F	150/80	11	14	Y	Y	N	N	N	N
42	CS	895606	52	F	160/80	15	6	N	N	N	Y	N	N
43	KK	707158	57	M	120/80	15	3	Y	N	N	N	N	Y
44	JS	912301	60	M	130/80	11	16	Y	Y	N	N	N	Y
45	SS	909515	61	F	160/90	15	4	Y	N	N	Y	N	N
46	JS	559784	68	M	110/80	11	16	N	N	N	N	N	N
47	VR	878486	55	F	130/80	15	4	Y	N	N	N	N	N
48	KK	888135	58	F	140/80	11	13	N	N	N	Y	N	N
49	GS	889423	56	M	140/80	9	21	Y	N	N	N	N	Y
50	JK	883398	85	F	130/70	7	27	N	Y	Y	N	N	N
51	KS	887749	59	M	140/80	7	21	Y	Y	N	N	N	Y
52	BS	893901	46	F	110/70	15	2	Y	N	N	Y	N	N
53	OP	480721	68	M	120/80	9	19	N	Y	N	N	N	N
54	KK	874853	80	M	130/80	10	21	N	Y	N	N	N	N
55	JS	916613	63	M	160/80	9	21	N	Y	N	N	N	N
56	SS	909450	55	F	130/80	15	4	N	N	N	N	N	N
57	NS	150360	36	M	140/80	15	2	N	N	N	N	N	Y
58	SK	914046	75	F	120/80	9	20	N	Y	N	N	N	N
59	JS	875306	58	M	130/80	15	2	N	N	N	N	N	Y

S NO	NAME					OUTCOME			
		BUN/Cr RATIO	LIPID PROFILE	URINE SPECIFIC GRAVITY	CT/MRI FINDING	DURATION OF STAY IN HOSPITAL	ICU REQUIRED	mRS GRADE	
							YES/NO	DAY 7 / DISCHARGE	DAY 30
1	BS	22.8	247/234/48/168	1.02	LT MCA INFARCT	12	Y	4	4
2	VK	16.9	200/190/45/150	1.015	LT MCA INFARCT	10	Y	4	4
3	KC	16.5	145/479/29/86	1.015	RT CEREBELLAR INFARCT	5	N	1	1
4	JS	17.6	230/200/40/160	1.01	BRAIN STEM INFARCT	2	Y	6	6
5	BM	16.8	64/203/29/45	1.015	RT MCA INFARCT	8	Y	5	6
6	HS	17.16	150/200/35/120	1.015	RT CEREBELLAR INFARCT	6	N	1	0
7	DM	14	123/80/36/74	1.015	LT MCA INFARCT	5	N	2	2
8	NS	11.6	140/110/45/100	1.01	LT ACA MCA INFARCT	10	Y	4	4
9	MS	20.3	200/210/38/140	1.02	POSTERIOR CIRCULATION INFARCT	2	Y	5	6
10	ML	18.5	206/163/36/134	1.018	RT MCA INFARCT	4	N	1	1
11	PL	18.7	240/121/53/177	1.015	POSTERIOR CIRCULATION INFARCT	7	Y	5	5
12	HS	10.9	170/200/35/100	1.01	RT FRONTO TEMPORAL PARIETAL INFARCT	4	N	0	0
13	BK	26.9	162/95/35/101	1.015	RT MCA INFARCT	7	N	2	2
14	SB	11.9	102/194/33/43	1.01	RT CORONA RADIATA INFARCT	7	N	2	2
15	GK	22.5	177/201/29/102	1.02	RT MCA INFARCT	3	Y	6	6
16	SS	17.5	100/146/31/50	1.015	RT CEREBELLAR INFARCT	3	N	1	0
17	K	22.8	236/302/35/144	1.02	LT PONTINE INFARCT	8	Y	3	3
18	HS	20.8	200/180/32/150	1.025	BRAIN STEM INFARCT	7	Y	4	4
19	KS	18.8	100/120/30/45	1.015	CEREBELLAR INFARCT WITH IVH	2	Y	5	6
20	RS	12.8	140/200/38/100	1.01	RT THALAMUS AND HIPPOCAMPUS	2	N	0	0
21	JS	26	105/140/30/80	1.02	LT MCA INFARCT	7	Y	4	4
22	JK	12.4	110/149/35/100	1.01	RT CEREBELLAR INFARCT	5	N	1	0
23	SM	16.21	183/119/31/134	1.015	RT MCA INFARCT	22	Y	4	4
24	MK	13	100/140/35/90	1.01	RT PARIETAL REGION BLEED	25	Y	4	4
25	MS	19.9	234/200/40/180	1.01	LEFT GANGIOCAPSULAR BLEED	20	Y	5	5
26	MK	13.2	240/200/30/140	1.01	PCA INFARCT	7	N	1	1
27	GK	9.6	110/180/33/80	1.01	RT MCA INFARCT	5	N	2	2
28	HS	16	167/66/52/110	1.015	RT MCA INFARCT	7	N	2	2
29	KS	10.4	184/108I/31/129	1.01	RT THALAMIC INFARCT	7	N	2	2
30	MS	25	234/270/30/180	1.02	BRAIN STEM INFARCT	10	Y	5	6
31	ZS	18.5	185/149/39/120	1.015	CORONA RADIATA INFARCT	5	N	1	0
32	AK	10.8	120/80/38/90	1.01	POSTERIOR CIRCULATION INFARCT	10	Y	4	4
33	NS	16.5	90/110/35/80	1.015	LT ACA INFARCT	5	N	1	0
34	MK	20	215/75/44/138	1.015	RT CEREBRAL INFARCT	3	N	1	0
35	PN	13.8	200/180/35/144	1.01	INFARCT PARIETAL OCCIPITAL REGION	5	Y	4	4
36	NS	18.6	110/100/28/100	1.02	FRONTAL LOBE INFARCT	7	N	3	3
37	KC	24.43	220/180/40/150	1.025	LT MCA INFARCT	5	Y	4	4
38	RS	12.46	237/200/34/180	1.01	RT MCA INFARCT	5	N	2	2
39	MS	18.29	129/67/41/100	1.015	LT MCA INFARCT	7	Y	4	4
40	RK	13.09	140/166/24/88	1.01	RT MCA INFARCT	8	N	2	2
41	KT	20.9	100/140/34/130	1.015	INFARCT LT FRONTAL AREA	22	Y	3	3
42	CS	10.8	112/97/29/72	1.01	RT MCA INFARCT	7	N	2	2
43	KK	9.5	100/120/33/80	1.01	LT CORONA RADIATA INFARCT	3	N	1	0
44	JS	17.9	150/211/31/92	1.01	INFARCT LT INTERNAL CAPSULE	10	Y	4	4
45	SS	20	230/200/44/180	1.015	INFARCT RT FRONTAL AREA	4	N	2	2
46	JS	16.7	165/147/39/110	1.015	LT MCA INFARCT	15	Y	4	4
47	VR	10.8	140/100/33/80	1.01	RT MCA INFARCT	5	N	1	1
48	KK	13.4	230/110/50/155	1.01	INFARCT LT FRONTAL AREA	8	Y	3	3
49	GS	21	250/200/34/190	1.025	LT MCA INFARCT	10	Y	4	4
50	JK	22.8	200/140/33/180	1.025	POSTERIOR CIRCULATION INFARCT	11	Y	5	5
51	KS	21.49	110/100/33/108	1.025	INFARCT LT MCA AND PCA TERRITORIES	14	Y	4	4
52	BS	16.28	237/139/35/170	1.015	INFARCT LT TEMPORAL AREA	4	N	1	0
53	OP	9.5	119/94/33/73	1.01	LT PONTINE INFARCT	29	Y	4	4
54	KK	22.8	100/80/33/110	1.02	LT MCA INFARCT	10	Y	4	4
55	JS	11.67	140/110/34/100	1.01	RT GANGLIOCAPSULAR BLEED	16	Y	4	4
56	SS	14.4	200/180/30/140	1.01	RT PCA INFARCT	6	N	2	2
57	NS	9.9	119/93/31/67	1.01	PONTINE INFARCT	3	N	1	0
58	SK	40.5	172/69/34/85	1.025	LT MCA INFARCT	14	Y	4	4
59	JS	12.6	110/140/33/80	1.01	RT PICA INFARCT	5	N	1	0

S NO	NAME	MRD NO	AGE	SEX				CO-MORBIDITIES AND PAST HISTORY					
					BLOOD PRESSURE	GCS	NIH STROKE SCALE	TYPE 2 DIABETES MELLITUS	HYPERTENSION	CORONARY ARTERY DISEASE	DYSLIPIDAEMIA	DIURETICS USE IN LAST 7 DAYS	H/O ANY ADDICTION
60	G	904312	64	M	180/90	11	16	N	Y	N	N	N	N
61	SK	905198	58	F	140/90	15	5	Y	N	N	N	N	N
62	SS	876737	57	M	160/80	9	23	N	Y	N	N	N	Y
63	GS	892698	58	M	130/80	11	18	N	N	N	N	N	N
64	RK	893389	60	F	170/90	7	22	N	Y	N	N	N	N
65	SS	874097	48	M	90/60	7	26	N	Y	N	N	N	Y
66	JK	973396	45	F	140/80	15	2	N	Y	N	N	N	N
67	VP	972131	62	F	120/80	15	8	Y	N	N	N	N	N
68	PS	78342	68	M	100/60	11	14	N	Y	N	N	N	N
69	SS	968666	85	F	140/80	7	21	Y	Y	Y	N	Y	N
70	AK	551563	55	M	160/80	11	16	N	Y	N	N	N	N
71	RS	305134	88	M	110/70	11	15	N	Y	Y	N	N	N
72	GK	967524	71	F	90/60	9	22	N	Y	N	N	N	N
73	PS	981646	62	M	160/80	15	1	N	Y	N	N	N	N
74	GS	146175	53	M	140/70	15	5	Y	N	Y	N	Y	Y
75	VK	153561	53	M	100/60	15	5	Y	Y	N	Y	N	Y
76	RK	962902	56	F	140/80	15	4	N	Y	N	Y	Y	N
77	MK	962603	64	M	110/70	15	6	N	Y	N	N	N	Y
78	BS	959094	46	M	110/70	15	3	N	N	Y	Y	N	Y
79	MS	959054	59	F	140/80	15	5	N	N	Y	N	Y	N
80	A	953717	58	M	110/70	11	16	Y	Y	N	Y	N	Y
81	SD	973308	79	F	140/80	9	19	N	Y	N	N	N	N
82	AS	980770	58	M	180/100	9	21	N	Y	N	N	N	N
83	KK	983492	54	F	110/70	15	3	N	N	Y	N	Y	N
84	SN	980914	58	F	110/70	15	4	Y	N	N	N	N	N
85	DK	974594	61	M	140/80	15	2	N	Y	Y	N	Y	Y
86	MR	975059	47	M	140/80	15	4	N	N	N	Y	N	Y
87	JR	979700	69	M	140/80	7	20	N	Y	Y	N	Y	N
88	DS	979023	58	F	110/70	15	4	N	Y	Y	N	Y	N
89	MH	977856	35	M	140/80	15	4	N	Y	N	N	N	Y
90	NK	448939	71	F	90/60	7	21	Y	Y	N	N	N	N
91	NR	424827	52	F	140/80	15	4	N	Y	Y	N	Y	N
92	SD	1001967	80	F	100/60	7	22	Y	Y	Y	N	Y	N
93	JK	878482	68	M	140/80	9	20	Y	Y	N	Y	N	N
94	SB	896375	52	M	120/70	15	3	N	N	Y	N	Y	Y
95	HS	153906	86	F	120/70	9	17	N	Y	Y	N	Y	N
96	ML	881325	70	M	180/100	11	18	N	Y	N	N	N	N
97	DG	899655	50	F	130/90	15	2	N	Y	N	N	N	N
98	RK	899170	60	M	120/80	15	2	Y	Y	N	Y	N	Y
99	BK	996211	80	F	100/70	7	26	N	Y	N	N	N	N
100	BK	995217	45	F	180/100	15	2	N	Y	N	N	N	N
101	JS	990820	47	M	200/110	11	16	N	Y	N	N	N	N
102	SS	973033	40	M	140/80	7	19	Y	N	N	N	N	N
103	SR	514681	46	F	140/80	15	3	N	N	N	Y	N	N
104	MS	985362	58	M	110/70	15	4	N	Y	N	N	N	Y
105	RS	986622	69	F	140/80	10	22	N	N	Y	N	Y	N
106	SK	592210	48	F	110/70	15	4	N	Y	N	N	N	N
107	SK	988313	65	F	120/80	11	17	Y	Y	Y	N	Y	N
108	SS	145296	56	M	130/80	15	5	N	Y	Y	N	Y	Y
109	GK	988103	57	M	150/80	11	14	N	N	N	N	N	N
110	PS	987786	49	F	140/80	11	12	N	Y	N	N	N	N
111	RK	982261	55	M	140/80	15	4	N	Y	N	N	N	Y
112	CL	969571	63	F	140/80	15	8	N	Y	N	N	N	N
113	BS	984320	55	M	130/80	15	6	N	Y	Y	Y	Y	Y
114	BK	878815	75	F	160/90	9	21	N	Y	N	N	N	N
115	DS	980262	59	M	140/80	11	16	N	Y	N	N	N	N
116	RK	984034	60	M	180/100	11	18	N	Y	N	N	N	N

S NO	NAME					OUTCOME			
		BUN/Cr RATIO	LIPID PROFILE	URINE SPECIFIC GRAVITY	CT/MRI FINDING	DURATION OF STAY IN HOSPITAL	ICU REQUIRED	mRS GRADE	
							YES/NO	DAY 7 / DISCHARGE	DAY 30
60	G	11.5	225/119/35/187	1.015	RT GANGLIOCAPSULAR BLEED	10	Y	4	4
61	SK	12.5	235/80/44/187	1.01	INTERNAL CAPSULE INFARCT	6	N	2	2
62	SS	18.5	188/71/72/111	1.025	LT GANGLIOCAPSULAR BLEED	14	Y	4	4
63	GS	16.8	140/110/32/80	1.01	RT GANGLIOCAPSULAR BLEED	10	Y	4	4
64	RK	10.2	166/199/28/113	1.01	POSTERIOR CIRCULATION INFARCT	12	Y	4	4
65	SS	22.19	220/160/44/110	1.01	MULTIFOCAL INFARCT	5	Y	5	6
66	JK	12.8	110/100/33/120	1.01	INFARCT RT PICA TERRITORY	5	N	1	0
67	VP	13.6	140/110/34/100	1.01	LT MCA INFARCT	6	N	2	2
68	PS	7.68	100/80/32/140	1.01	RT MCA INFARCT	10	Y	3	3
69	SS	24	118/100/33/140	1.025	LT MCA INFARCT	12	N	5	5
70	AK	16.29	120/100/33/140	1.01	LT GANGLIOCAPSULAR BLEED	15	Y	4	4
71	RS	20.97	200/140/34/110	1.01	CORONA RADIATA INFARCT	7	N	4	4
72	GK	10.3	226/65/56/148	1.01	POSTERIOR CIRCULATION INFARCT	15	Y	4	4
73	PS	12.6	204/199/27/149	1.01	RT MIDDLE CEREBELLAR PEDUNCLE INFARCT	5	N	1	0
74	GS	25	147/165/33/90	1.025	RT MCA INFARCT	6	N	2	2
75	VK	22.4	180/100/45/100	1.03	LT MCA INFARCT	10	N	2	2
76	RK	18	149/144/38/86	1.015	CORONA RADIATA INFARCT	4	N	1	0
77	MK	10.5	95/106/22/57	1.01	RT MCA INFARCT	6	N	2	2
78	BS	14	202/132/34/148	1.01	LT MCA INFARCT	6	N	1	1
79	MS	12.2	104/99/29/59	1.01	RT MCA INFARCT	8	N	2	2
80	A	19.94	174/123/40/121	1.025	LT MCA INFARCT	20	Y	3	3
81	SD	10	110/100/33/140	1.01	RT CEREBELLAR HAEMORRHAGE	8	Y	4	4
82	AS	13.5	180/110/32/100	1.01	RT GANGLIOCAPSULAR BLEED	20	Y	4	4
83	KK	18	88/100/32/120	1.015	CORONA RADIATA INFARCT	5	N	1	0
84	SN	7.7	149/88/32/100	1.012	RT MCA INFARCT	4	N	1	1
85	DK	16.82	146/100/67/65	1.015	RT CEREBELLAR INFARCT	4	N	1	0
86	MR	12.8	220/140/33/180	1.01	LT MCA INFARCT	6	N	1	1
87	JR	18.6	180/120/33/140	1.02	INFARCT B/L CEREBELLAR HEMISPHERE	5	Y	5	6
88	DS	17.52	220/200/38/110	1.02	RT MCA INFARCT	5	N	1	1
89	MH	12.8	100/120/33/140	1.01	RT THALAMIC INFARCT	7	N	2	2
90	NK	21.73	170/100/40/150	1.025	LT MCA INFARCT	20	Y	6	6
91	NR	11.2	100/140/33/100	1.01	INFARCT LEFT FRONTAL LOBE	6	N	2	1
92	SD	16.47	160/128/34/100	1.02	LT MCA INFARCT	16	Y	5	5
93	JK	28	110/100/32/80	1.03	INFARCT RT MCA ACA TERRITORY	13	Y	4	4
94	SB	10.8	102/194/33/43	1.01	INFARCT RT CORONA RADIATA	5	N	2	2
95	HS	16.37	180/110/33/100	1.015	LT MCA INFARCT	40	Y	5	5
96	ML	17.6	110/100/33/140	1.01	LT THALAMIC BLEED WITH IVH	10	Y	4	4
97	DG	9.7	154/114/54/83	1.01	THALAMIC INFARCT	5	N	2	1
98	RK	13.5	164/110/32/100	1.01	LT MEDULLARY INFARCT	3	N	1	0
99	BK	14	144/110/39/82	1.01	INFARCT LT MCA +ACA TERRITORY	8	Y	5	6
100	BK	14.2	110/100/33/80	1.01	LT CEREBELLAR INFARCT	5	N	1	0
101	JS	21.7	140/80/34/100	1.01	RT GANGLIOCAPSULAR BLEED	15	Y	4	4
102	SS	30.2	102/80/24/88	1.03	POSTERIOR CIRCULATION INFARCT	40	Y	5	5
103	SR	12.5	180/110/34/100	1.01	LT PCA INFARCT	6	N	1	0
104	MS	12.5	200/180/44/100	1.01	RT MCA INFARCT	5	N	2	2
105	RS	25.4	130/100/33/88	1.03	LT MCA INFARCT	10	Y	4	4
106	SK	11.6	200/180/33/140	1.01	LT MCA INFARCT	4	N	1	0
107	SK	20.7	108/100/34/80	1.02	LT MCA INFARCT	20	Y	4	4
108	SS	10.9	130/120/49/73	1.01	POSTERIOR CIRCULATION INFARCT	7	N	2	2
109	GK	17.2	189/75/54/129	1.01	RT MCA INFARCT	8	Y	3	3
110	PS	9.9	130/67/57/75	1.01	LT MCA INFARCT	6	N	3	3
111	RK	13.35	140/74/30/104	1.01	POSTERIOR CIRCULATION INFARCT	8	N	2	2
112	CL	12.8	152/144/30/113	1.01	LT MCA INFARCT	6	N	2	2
113	BS	12.3	124/90/40/70	1.01	CORONA RADIATA INFARCT	5	N	2	1
114	BK	21.2	180/142/44/150	1.02	RT GANGLIOCAPSULAR BLEED	10	Y	4	4
115	DS	17.7	93/50/30/55	1.01	LT MCA INFARCT	12	Y	4	4
116	RK	9.9	104/88/44/90	1.01	LT GANGLIOCAPSULAR BLEED	16	Y	4	4

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Date 20/4/2021

The Principal,
DMC,Ludhiana

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of **Amandeep Kaur,** a student of your college for **MD General Medicine** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Correlation of bun/creatinine ratio with outcome in acute stroke

Supervisor
Dr. Dinesh Jain
Prof.,
Dept. of Medicine,
DMCH, Ludhiana.

Co-Supervisor
Dr. Birinder Singh Paul
Prof.,
Dept. of Neurology,
DMCH, Ludhiana.
Dr. Amit Bery
Assoc. Prof.,
Dept. of Medicine,
DMCH. Ludhiana.

The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

S P Singh
Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. ***If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.***
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

CORRELATION OF BUN/CREATININE RATIO WITH OUTCOME IN ACUTE STROKE

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DOCTOR OF MEDICINE

In

MEDICINE

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

NOVEMBER 2019

DR. AMANDEEP KAUR

DEPARTMENT OF MEDICINE

DAYANAND MEDICAL COLLEGE AND HOSPITAL

LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	Correlation of BUN/Creatinine ratio with outcome in acute stroke
For the degree of	M.D.Medicine
Name of the candidate	Dr. Amandeep Kaur
Supervisor	Dr. Dinesh Jain, Professor, Department of Medicine, DMC&H, Ludhiana
Co-supervisor	Dr. Birinder Singh Paul, Professor, Department of Neurology, DMC&H, Ludhiana Dr. Amit Bery, Associate Professor , Department of Medicine , DMC&H, Ludhiana
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Stroke is becoming an important cause of premature death and disability in low income and middle income countries like India. Hydration status at the time of stroke has been acknowledged as an important determinant in early stroke recovery. During the early stroke recovery period, autoregulatory systems are impaired, leaving the brain vulnerable to blood viscosity and pressure changes that could further injure the area already compromised by decreased oxygen and nutrients. A common marker used for assessment of dehydration is the blood urea nitrogen to creatinine ratio (BUN/Cr ratio).

Aim of Study: To correlate BUN/Creatinine ratiowith outcome in acute stroke.

Materials & methods: An observational prospective study of all patients with acute stroke presenting to Emergency department of Dayanand medical college and hospital from January 2020 to December 2020 after fulfilling the inclusion and exclusion criteria will be included in the study.

Clinical Significance: To determine if BUN/Creatinine ratio of >15 at admission, is an independent risk factor for poor outcome in patients presenting with acute stroke. Dehydration being a treatable condition, the use of BUN/Creatinine > 15 as a marker of dehydration, can be helpful in detecting patients with dehydration early and thus may play a role in improving outcome of stroke patients.

Keywords: Blood urea nitrogen/Creatinine ratio, acute stroke, outcome.

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled"**CORRELATION OF BUN/CREATININE RATIO WITH OUTCOME IN ACUTE STROKE**"exist in the Department of Medicine, Dayanand Medical College and Hospital, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected bythe candidate himself/herself under our supervision and guidance.

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Co-Supervisor

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Dr. Amit Bery
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Head of the Department

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Place: _____

Date: _____

APPROVAL PROFORMA
BYRESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Amandeep Kaur
Department	Medicine
Topic of Thesis	Correlation Of Bun/Creatinine ratio With Outcome In Acute Stroke
Likely date of appearing in PG examination	June 2022
Date of enrollment	1st MAY,2019
Name of Head of Department	Dr. Dinesh Gupta
1) Supervisor **2) Co-Supervisor**	1) Dr.Dinesh Jain 2) Dr.Birinder Singh Paul 3) Dr. Amit Bery
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Jaspal Singh (Professor & Head, Surgery)	Mr. A K Jindal (Member, Ethics Committee)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Assistant Dean Academics)	Dr. Deepinder K Chhina (Professor & Head, Microbiology)
Dr. Rajoo Singh Chhina (Dean Academics)	Dr. Neena Sood (Professor & Head, Pathology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)
Approved: Yes / ~~No~~	**Approved: Yes / ~~No~~**

Dr. Sandeep Puri
Chairperson
Research Committee

Chairperson
Research Committee

Prof. Arvind Malhotra
Chairperson
Ethics Committee

Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. Amandeep Kaur VPOMiani, Ward No.4 Hoshiarpur
2	NAME OF THE INSTITUTE	Dayanand Medical College and Hospital
3	COURSE OF STUDY AND SUBJECT	M.D. MEDICINE
4	DATE OF ADMISSION OF COURSE	1st MAY,2019
5	TITLE OF THE TOPIC	Correlation of bun/creatinine ratio with outcome in acute stroke

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Stroke is becoming an important cause of premature death and disability in low-income and middle-income countries like India, largely driven by demographic changes and enhanced by the increasing prevalence of the key modifiable risk factors.[1]Stroke accounts for almost 5% of all disability-adjusted life-years and 10% of all deaths worldwide, with the bulk of this burden (>75% of deaths from stroke and >80% of disability-adjusted life-years) occurring in low-income and middle-income countries.[2]

Early neurological deterioration is common, occurring in 26–43% of patients, and about half of all cases occur within 24 h of admission.[3] Amongst markers of relative dehydration, BUN/Creatinine >15 at admission was found to be an independent risk factor for END, as also Urine specific gravity > 1.010.[4]

Adequate hydration status is important to maintain physiological homeostasis in humans. The brain is able to control cerebral blood flow through autoregulation allowing constant cerebral perfusion pressure despite moderate variations of blood pressure.[5]

Dehydration is not an uncommon finding of patients presenting to an emergency department with an overall prevalence of 7%. It is more common in elderly patients with one estimate suggesting 1.5% of independent elderly patients will be admitted for dehydration annually and evidence of chronic dehydration can be seen in almost half of geriatric patients presenting to emergency departments for care.[5]

A large percentage of stroke patients are dehydrated at the time of stroke and appear to have worsened functional outcomes.Dehydration might adversely affect the acute stroke patient in several ways: (1) reduced brain perfusion (2) increased fatigue (3) impaired neuroplasticity. During the early stroke recovery period, autoregulatory systems are impaired, leaving the brain vulnerable to blood viscosity and pressure changes that could further injure the area already compromised by decreased oxygen and nutrients. Dehydration

increases blood viscosity and is felt to diminish cerebral blood flow due to lower intravascular volume.[6]

Next, the functional consequences of dehydration during the early stroke recovery period could include: increased rates of delirium, poor concentration, increased fatigue, or positional hypotension. These early functional consequences may be crucial since neuroplasticity is thought to peak in the first several weeks after stroke, so engagement in physical therapy during this limited period is critical Hydration status at the time of stroke has been acknowledged as an important determinant in early stroke recovery BUN/creatinine ratio > 15 has been used most commonly in stroke hydration research and appears to be a reasonable choice for use in future research specifc to hydration and stroke outcome.[6]

The development of collateral flow after occlusion of major arteries can sustain brain tissue for hours and may play a role in maintaining perfusion in the penumbral region. Dehydration would lower the overall and cerebral blood volume, the blood velocity as well as the intravascular pressure that results in a lower pressure gradient and the ability to stimulate collateral recruitment.[7]

Though yet unproven, there are several biological theories about why a Volume contracted state (VCS) at the time of stroke could influence functional outcome. These include reduction of cerebral perfusion during critical periods of failing autoregulation, increased overall viscosity disrupting microcirculatory pathways, and the dilution and circulation of inflammatory cells that may accelerate cerebral edema in the region of infarction.[8]

6.2 REVIEW OF LITERATURE

Pandian et al studied the burden of stroke and the availability of health Services in India. The estimated adjusted prevalence rate of stroke range, 84-262/100,000 in rural and 334-424/ 100,000 in urban areas. The incidence rate is 119-145/100,000 based on the recent population based studies. There is also a wide variation in case fatality rates with the highest being 42% in Kolkata. Stroke units are predominantly available in urban areas that too in private hospitals.[1]

Global Burden of Disease (GBD) 2016 study estimates to provide global, regional, and country-specific lifetime risk of stroke in 1990 and 2016 by pathological subtype, age, sex and Socio-Demographic Index (SDI), accounting for competing risk of mortality due to all other non-stroke causes of death.The global estimated lifetime risk of stroke from age 25 onward was 24.9%: 24.7% in men and 25.1% in women. Globally from 1990 to 2016, there was a significant increase in the average lifetime risk of stroke from 22% to 24%, a relative increase of 9% .[2]

Kwan J, Hand P study demonstrated that patients with early neurological deterioration were significantly more likely to: (i) arrive at the hospital earlier (ii) have a history of atrial fibrillation (iii) be current non-smokers (iv) have a severe stroke-more total anterior circulation strokes and worse NIHSS and GCS scores; (v) have intracerebral haemorrhage (vi) have higher serum urea and leukocyte count and (vi) die in hospital .[3]

Bhatia K et al study concluded that National Institutes Health Stroke Scale score (NIHSS) ≥ 12 at admission is an independent risk factor for END (Early neurological deterioration).Amongst markers of relative dehydration, BUN/creatinine >15 at admission was found to be an independent risk factor for END, as also USG >1.010. Also, cerebral oedema and size of hypodensity >1/3rd of the middle cerebral artery territory on cranial CT were observed to be independent risk factors for END.[4]

Schrock JW et al studied association of elevated BUN/Creatinine with outcome in AIS. The variables associated with a poor clinical outcome

were: high NIHSS OR 6.5 (3.6-11.8), age >64 years OR 2.7 (1.5-5.0), and BUN/Cr ratio of ≥15 OR 2.2 (1.2-4.0).[5]

Mona N. Bahouthet al conducted Twenty-five studies of 8699 acute stroke patients. Overall, rates of dehydration in the acute stroke population ranged from 29 to 70% using a variety of measurement techniques. The most common laboratory markers used in these studies was blood urea nitrogen to creatinine ratio (BUN/Cr) which was used in 12 studies.Of the 12 studies reporting patient outcomes, 10 (83%) reported worse clinical outcomes in dehydrated stroke patients. BUN/creatinine ratio > 15 has been used most commonly in stroke hydration research and appears to be a reasonable choice for use in future research specifc to hydration and stroke outcome .[6]

Chang SW et al studied the association of development of leptomeningeal collaterals after acute MCA occlusion with the patient's hydration status. The development of PCA laterality and HVs shows a significant difference between dehydrated and euhydrated patients. Dehydration remained an independent negative predictor for the development of PCA laterality and HVs in the multivariate analysis.[7]

Bahouth, Mona N et al studied the relationship between a volume contracted state (VCS) at the time of ischemic stroke and hospital outcomes as compared with euvolemic patients. Acute stroke patients in a VCS demonstrate worse short-term outcomes compared to euvolemic patients, independent of infarct size. VCS was defined via surrogate markers (blood urea nitrogen/creatinine ratio >15 and urine specific gravity >1.010). 42% of patients in a VCS demonstrated early clinical worsening, compared with 17% of the euvolemic group (p = 0.02).[8]

Mohammad Dehghani-Firoozabadi study demonstrated that patients who succumbed to Stroke (early death or late death) had significantly higher mean BUN, BUN/Cr levels than those who survived. This correlation of hyperuremia and mortality suggests that it may be usefulin guiding risk assessment and treatment of stroke.[9]

Liu CH, Lin SC, Lin JR et al studied the influence of admission dehydration on the discharge outcome in acute ischaemic and

hemorrhagic stroke.Acute ischaemic stroke with admission dehydration had higher infection rates, worse discharge Barthel index, worse mRS and higher admission costs than those without dehydration.[10]

Bahouth MN et al study demonstrated that patients who are in a volume contracted state at the time of presentation with stroke have more severe hemispatialneglect. Elevated BUN/Creatinine ratio was associated with an increased odds of severe neglect in unadjusted models, with loss of significance in adjusted models (OR 4.43, (95% CI 0.99, 19.8) after adjustment for age, infarct volume, sex, and NIHSS score.[11]

Bhatia R S et al study demonstrated that among hematological parameters, high total leukocyte count and ESR, at admission, correlated significantly with an undesirable outcome during the initial 30 days. Among biochemical parameters, elevated urea, creatinine, serum transaminases (SGOT and SGPT) and globulin levels correlated significantly with death.[12]

You S, Zheng D et al evaluated and compared the prognostic significance of BUN and other CKD biomarkers (eGFR, Cr and BUN/Cr) in in-hospital mortality and poor discharge outcomes after AIS. The BUN was independently associated with all-cause in-hospital mortalitybut not poor outcome at discharge. [13]

Bhalla A, Sankaraling am S et al studied the association of raised plasma osmolality on stroke outcome at 3 months and the change of plasma osmolality with hydration during the first week after stroke. Mean admission (300 mOsm/kg, SD 11.4), maximum (308.1 mOsm/kg, SD 17.1), and Area under curve (296.3 mOsm/kg, SD 11.7) plasma osmolality were significantly higher in those who died compared with survivors.[14]

Rodriguez GJ, Cordina S Met at study observed a higher plasma osmolality among elderly patients with cerebral ischaemic events who present within 24 h of symptom onset compared with controls from the general population. This seems to be an early phenomenon and possibly a contributing factor to cerebral ischemia..[15]

Rowat A, Graham C et al study demonstrated that patients with dehydration within 1 day of admission(n927) and those with dehydration at any stage of theiradmission (n1606; Table 2) were both significantly more likely to be older, to be female, to have a total anterior circulation syndrome, to be prescribed diuretics, to require parenteral fluids and/or enteral tube feeding, and were predicted to be less likely to be alive/independent in daily activities at 6 months (based on their baseline features) than those who were not dehydrated.[16]

Alawneh JA, Moustafa RR et al study demonstarted that Hemodynamic factors and perfusion abnormalities are likely to play a critical role in END. Infarction of the oligemic tissue surrounding the penumbra could be the putative culprit leading to END as a result of perfusion, but also physiological and biochemical abnormalities.[17]

Lin LC, Yang JT et al study demonstrated that an initial National Institutes of Health Stroke Scale score of 12 or higher, a Glasgow Coma Scale score of 12 or lower, d-dimers more than 1000, or blood urea nitrogen/creatinine (BUN/Cr) ratio higher than 15 were more frequent in SIE(stroke in evolution) patients. After multivariate analysis, only a BUN/Cr higher than 15 was independent predictor of SIE.[18]

Crary MA et al studied nutrition and hydration status in ischemic stroke patients with versus without clinically significant dysphagia at admission and at discharge from acute care. At admission 32 % of patients demonstrated malnutrition based on prealbumin levels and 53 % demonstrated evidence of dehydration based on BUN/Cr levels.[19]

The National Institute of Neurological and Communicative Disorders and Stroke initiated the Stroke Data Bank, which is a multicenter project to prospectively collect data on the clinical course and sequelae of stroke.. Additional objectives were to provide information that would enable a standard diagnostic clinical evaluation, to identify prognostic factors, and to provide planning data for future studies.[20]

6.3 AIMS AND OBJECTIVES OF THE STUDY

- To correlate BUN/Creatinine ratio with outcome in acute stroke.

7. MATERIALS AND METHODS

All patients presenting to Emergency department of Dayanand Medical College and Hospital with acute stroke from January 2020 to December 2020 after fulfilling the inclusion and exclusion criteria will be included in the study.

Diagnosis of stroke will be made by WHO definition of stroke as ' a clinical syndrome consisting of rapidly developing clinical signs of focal (or global in case of coma) disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than a vascular origin. The further subtyping of stroke will be done by Radiology department. The following details will be collected: age; sex; signs and symptoms; Glasgow coma scale (GCS), history of diabetes, hypertension, coronary artery disease, dyslipidaemia, diuretic use and smoking habits. Laboratory investigations comprising complete blood count with haematocrit, blood urea, serum creatinine, BUN/creatinine ratio, serum electrolytes, blood glucose at admission, plasma osmolality (calculated), lipid profile, urine specific gravity, brain imaging and electrocardiogram within 24 h of admission in all the patients. BUN/creatinine ratio will assessed at the time of admission with regular assessment on day 3 and 5. Since BUN reflects only the nitrogen content of urea (MW 28) and urea measurement reflects the whole of the molecule (MW 60), urea is approximately twice (60/28 = 2.14) that of BUN. Following formula will be used , Urea [mg/dL]= BUN [mg/dL] * 2.14. Factor = 1 for conversions in mmol (1 mole N_2 = 2 moles N per mole of urea). The neurological status of the patient and the severity of stroke will be assessed by using the NIHSS scoring system. Evaluations will be performed immediately at the time of admission, and then subsequently on day 2, day 3 and on discharge.

7.1 SOURCE OF DATA

Emergency department at Dayanand Medical College and Hospital, Ludhiana.

7.2 METHOD OF COLLECTION OF DATA

Consecutive patients presenting to Emergency department of Dayanand medical college and hospital with stroke after fulfilling the inclusion and exclusion criteria will be included in the study

INCLUSION CRITERIA

- Patients>18 years age
- Acute stroke (ischaemic / hemorrhagic) < 24 hours duration
- Patient/attendant willing to give informed written consent

EXCLUSION CRITERIA

- Stroke > 24 hours duration
- Transient ischaemic attack
- Stroke mimics
- Congestive cardiac failure
- Chronic kidney disease
- Decompensated cirrhosis of liver

OUTCOME

Outcome will be assessed by mRS grading on day 7th / discharge and day 30th(on telephone)

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate.For comparing categorical data, Chi square ($\chi 2$) test will be performed and exact test was used when the expected frequency is less than 5. A probability value (p value)less than 0.05 will be considered statistically significant. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Yes this study requires biochemical and radiological investigations.

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

8. LIST OF REFERENCES

1. Pandian JD, Sudhan P. Stroke epidemiology and stroke care services in India. Journal of stroke. 2013;15:128-34.
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17. AlawnehJA, Moustafa RR, Baron JC. Hemodynamic factors and perfusion abnormalities in early neurological deterioration. Stroke. 2009;40:e443-50.
18. Lin LC, Yang JT, Weng HH, Hsiao CT, Lai SL, Fann WC. Predictors of early clinical deterioration after acute ischemic stroke. The American journal of emergency medicine. 2011;29:577-81.
19. Crary MA, Humphrey JL, Carnaby-Mann G, Sambandam R, Miller L, Silliman S. Dysphagia, nutrition, and hydration in ischemic stroke patients at admission and discharge from acute care. Dysphagia. 2013;28:69-76.

20. Foulkes MA, Wolf PA, Price TR, Mohr JP, Hier DB. The Stroke Data Bank: design, methods, and baseline characteristics. Stroke. 1988;19:547-54.

20. Foulkes MA, Wolf PA, Price TR, Mohr JP, Hier DB. The Stroke Data Bank: design, methods, and baseline characteristics. Stroke. 1988;19:547-54.

PROFORMA

S NO.

NAME MRD NO

AGE SEX

FATHER'S NAME

ADDRESS

PHONE NO.

FINAL DIAGNOSIS

GENERAL PHYSICAL EXAMINATION

PULSE RATE BLOOD PRESSURE

RESPIRATORY RATE TEMPERATURE

SO2 PALLOR

ICTERUS LYMPHADENOPATHY

CYANOSIS EDEMA

JVP CLUBBING

GCS ON ADMISSION

EYE

VERBAL

MOTOR

SYSTEMIC EXAMINATION

- CENTRAL NERVOUS SYSTEM -

  Neurological examination sheet attached

- CARDIOVASCULAR SYSTEM –
- RESPIRATORY SYSTEM –
- PER ABDOMEN –

CO MORBIDITIES–

DIABETES MELLITUS TYPE 2

HYPERTENSION

CORONARY ARTERY DISEASE

DYSLIPIDAEMIA

TREATMENT HISTORY OF LAST 7 DAYS

H/O ANY ADDICTION

LABORATORY INVESTIGATIONS –

CBC

S. ELECTROLYTES

S. UREA

S. CREATININE

BUN/CREATININE RATIO

LIPID PROFILE

URINE SPECIFIC GRAVITY

CT/MRI FINDING

Signature of Candidate

Signature of Supervisor

OUTCOME –

DURATION OF STAY IN HOSPITAL

ICU REQUIRED YES/NO

NIH STROKE SCALE DAY 1 DAY 2 DAY 3 AT DISCHARGE

mRS GRADE DAY 7 / DISCHARGE DAY 30

(ON TELEPHONE)

mRS GRADING

0 - No symptoms at all

1 - No significant disability despite symptoms; able to carry out all usual duties and activities

2 - Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance

3 - Moderate disability; requiring some help, but able to walk without assistance

4 - Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance

5 - Severe disability; bedridden, incontinent and requiring constant nursing care and attention

6 - Dead

Signature of Candidate **Signature of Supervisor**

DAYANAND MEDICAL COLLEGE & HOSPITAL
LUDHIANA

NEUROLOGICAL EXAMINATION SHEET

Physical Appearance (e.g. nutrition, cleanliness body-build, ethnic group, physiological age, congenital abnormalities, posture, facies, anaemia, jaundice, cyanosis, etc).

Mental state (e.g. personality, reliability, co-operation, mood, cognitive and intellectual functions memory, etc.) (See Annexure-I).

Speech

Expression :
Comprehension :
Repitition :
Reading :
Writing :
Paraphasias :
Naming Objects :

Simple :

Complex :

Skull (e.g. skull contours, measurements symmetry, tenderness, precussion, cranial or orbital bruit, etc.)

Spine (e.g. deformity, limitation of movement, tenderness, nuchal rigidity etc.)

Gait and Stance (e.g. shuffling, festinating, ataxic, broad base, spastic, high-stepping, pro-or retropulsion, Romberg's sign etc.)

Cranial Nerve Examination

Cranial Nerve 1

1. Odours Perceived

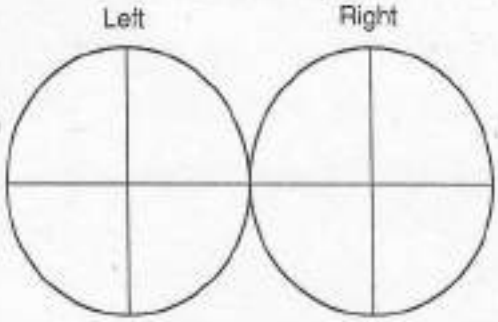
R	L

1. Visual Acuity

	R	L
Distance — Uncorrected		
Distance — Corrected		
Reading — Uncorrected		
Reading — Corrected		

Cranial Nerve 2

Visual Fields (by confrontation or other methods, noting central, peripheral and attention defects.



Fundi (media, disc, retina & vessels, macula)

Cranial Nerve 3,4 & 6

Pupils

		R	L
Size			
Shape			
Reaction to light	Direct		
	Consensual		
Reaction to convergence			

Ocular movements, diplopia
Ptosis, Ex-or enophthalmos, lid-lag etc.

Nystagmus (Grade, Unilateral or Bilateral, Primary position or gaze evoked, direction)

Cranial Nerve 5

	R	L
Masseter		
Temporalis		
Jaw Opening		
Corneal Reflexes Direct		
Consensual		

Cranial Nerve 9 & 10

Swallowing	
Phonation	
Palatal Movement	
Gag reflex	

Tonsillar fossa, Posterior pharyngeal

Cranial Nerve 7

Facial Symmetry		
	R	L
Weakness		
Taste (ant. 2/3)		

Abnormal movements

Cranial Nerve 11

		R	L
Sternomastoids	bulk		
	power		
Trapezius	bulk		
	power		

Cranial Nerve 8

	R		L	
Hearing				
Rinne's test	AC	BC	AC	BC
Webers Test				

Cranial Nerve 12

Tongue protrusion		
Fibrillations	R	L
Movement: range, speed		
Appearance		

Motor System (Abnormal position, tone, wasting, fasciculations and motor power)

Deep Tendon Reflexes

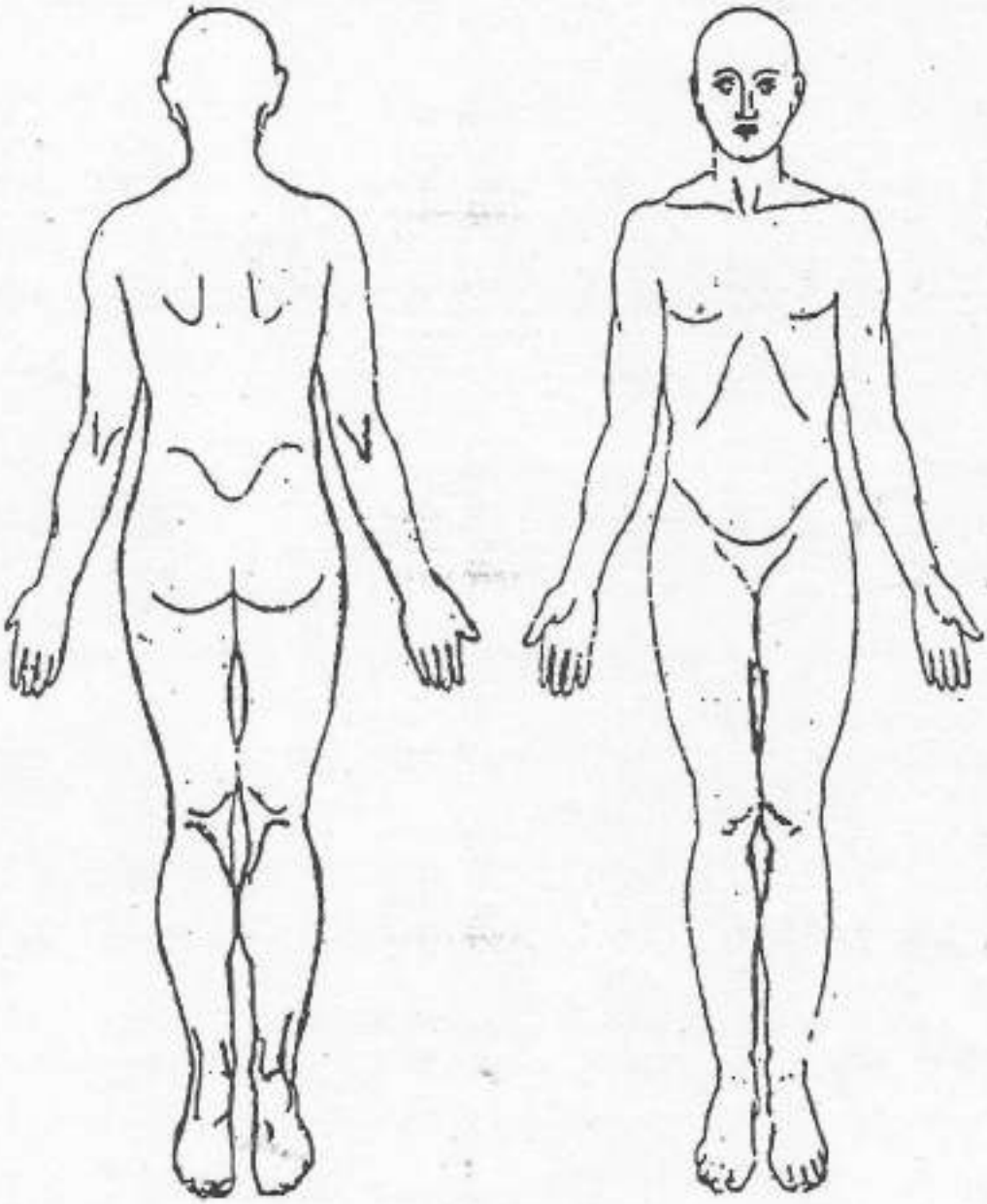
	Right	Left		Right	Left
Jaw Jerk			Knee		
Biceps			Ankle		
Supinator			Finger flexion		
Triceps			Others		

Reference:- ++++ = Clonus
+++ = very brisk; ++= brisk;+=present; ± with reinforcement; - = absent;

Superficial reflexes

	Right	Left
Abd. Upper		
Abd. Lower		
Cremasteric		
Plantars		

Sensory System: - (Use sensory charts where possible, palpate peripheral nerves) temperature; light touch; position sense; vibration; deep pain; 2 point discrimination; stereognosis; figure - writing; sensory inattention)



INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....
.....am willing to participate in the study**"CORRELATION OF BUN/CREATININE RATIO WITH OUTCOME IN ACUTE STROKE"**The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य "**CORRELATION OF BUN/CREATININE RATIO WITH OUTCOME IN ACUTE STROKE**"में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ

_____"COR RELATION OF BUN/CREATININE RATIO WITH OUTCOME IN ACUTE STROKE" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ-ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ

_____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ